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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 38.] 1941. [No. 6.

SUMMARY OF RECENT ABSTRACTS.*

V. LEISHMANIASIS.

VISCERAL.

Epidemiology.

MATTEI *et al.* (p. 349) report two cases of kala azar in adults in Corsica, where the disease is usually only found in children. They suggest that the disease in adults may be more common than has been suspected. The village from which one of these patients came was known to be an endemic focus of infantile and canine kala azar and a dog belonging to the patient was diagnosed as suffering from the disease. The patient stated that she had been bitten by a tick and the authors maintain that these facts support their contention that the dog is a reservoir and the tick the vector of the disease. CELIK (p. 767) also reports kala azar in an adult (the first recorded case) from an area in which it is endemic in children in Turkey.

MORNET (p. 768) records the first discovered case of kala azar in a dog in the Niger territory, though a number of cases have been seen in Dakar. MALBRANT (p. 768) has reported the first three dogs found to be infected with kala azar in Brazzaville.

Aetiology.

ALEKSEJEV and KONAKHOV (p. 345) find no evidence of multiplication of leishmania other than by binary fission after the destruction of the macrophages which have engulfed them. They regard *Leishmania donovani*, *L. infantum* and *L. tropica* as "good species" on epidemiological but not on morphological grounds.

ADLER (p. 768) inoculated 5 patients, who were suffering from inoperable carcinoma, with massive doses of cultures of *L. donovani*;

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1940, Vol. 37. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

only one patient became infected, and though the infection was heavy, no symptoms of kala azar developed during a period of 9 months' observation.

WANG and CHUNG (p. 769) found that susceptibility to intraperitoneal injection of culture forms of *L. donovani* was increased in hamsters by splenectomy or by the injection of benzol and olive oil before the injection of the flagellates.

CHUNG and WANG (p. 769) report work in which infection with *L. donovani* in hamsters, cured by neostibosan, appeared to give protection against subsequent infection with *L. canis* from a naturally infected dog. This suggests that human and canine strains in N. China are either identical or closely related. [There is increasing evidence that in N. China, as in the Mediterranean, the dog is the reservoir host of the human disease, see this *Bulletin*, 1940, Vol. 37, p. 389.]

Transmission.

SMITH *et al.* (p. 769) show that when *Phlebotomus argentipes* were offered a blood meal 10 days after an infective meal, some of the flies made unsuccessful attempts to suck blood. Dissection of these flies showed that, as in the case of fleas infected with plague bacilli, there was complete blockage of the oesophagus, and it would seem probable that in the efforts to feed, some of the flagellates must be dislodged and could then readily pass into the skin. The authors have found that flies are kept alive after an infective feed more readily by allowing them to feed on raisins than by giving them successive blood meals, and these observations may afford a clue to the reason why it has been so difficult to transmit infection by flies which have been given repeated blood meals.

KIRK and LEWIS (p. 770) show that of the 13 species of Phlebotomus recorded from the Sudan, *P. langeroni* var. *orientalis* is the only member of the "*major* group," and that all the places in which it has been found are within the area in which kala azar is endemic. It may be found as far as 5 miles from human habitations.

YUAN *et al.* (p. 346) show that in children in N. China infection appears to take place in the early summer months, a period which corresponds to the greatest incidence of *Phlebotomus chinensis*, specimens of which were found to be naturally infected during June and July in kala azar houses.

JOYEUX and SAUTET (p. 346) give reasons for the supposition that under certain conditions the dog louse, *Linognathus setosus*, may be able to transmit kala azar from dog to man.

Pathology.

At post mortem examination of patients (suffering from inoperable carcinoma) who were given massive injections of leishmania, ADLER (p. 768) found two types of cell infection: in one the cytoplasm was filled with parasites (Kupffer cells and splenic reticular cells), in the other the parasites were few (arterial adventitia cells, Glisson's capsule and others). Though the cells of the first type were filled with parasites, they were still capable of phagocytosis. DHAR (p. 348) has found that pneumonia is a much more serious disease in persons with kala azar than when it attacks healthy persons. He considers that this is probably due to the loading of the reticulo-endothelial system by the

parasites. Treatment of the underlying condition is important. MURANO and VECCHIO (p. 348) have found that in rabbits with a blocked reticulo-endothelial system the serological response to injections of typhoid vaccines is better than in normal controls, and that the same is true of children with kala azar, in whom the reticulo-endothelial system may be presumed to be hypertrophied and blocked with leishmania. The authors consider that these facts support the view that immune bodies are products of the cells of the reticulo-endothelial system and that they are increased in leishmaniasis because of the hypertrophy and hyperplasia of the histioid cells of that system. Expanding this point, in infantile kala azar, MURANO (p. 770) states that his work indicates that increased production of complement is associated with hyperplasia of the histiocytes, but that leucocytes do not play any part, since there is no relationship between the amount of complement and the number of leucocytes present in the blood. An increase in complement, therefore, does not mean an increase in the defensive mechanism of the body, which in kala azar is very susceptible to intercurrent infections.

BOTZARIS (p. 347) has studied the blood changes in infantile kala azar in Greece.

Clinical.

KIRK and SATI (p. 771) find that in the Sudan superficial skin papules or ulcers, containing leishmania, are often seen in kala azar. Leishmania are rare in blood smears but the authors found them in gland puncture material in each of 30 consecutive cases. In recording this important finding they describe in detail the technique used; the glands along the saphenous vein are punctured with a *dry* hypodermic needle without a syringe, and the juice which enters the needle is blown on to a slide and stained.

NAPIER (p. 349) discusses the diagnosis of kala azar in dispensary practice. Spleen puncture is the best method for discovery of the parasites. If parasites cannot be found and serological tests are doubtful and do not show signs of becoming positive after one month, the case is probably not one of kala azar. In N. China YOUNG (p. 771) found spleen puncture to be almost invariably positive in kala azar; liver puncture is useful also, but the search for parasites in nasal mucus was negative in 26 cases examined. He points out that in making smears the heavily infected cells tend to break and the leishmania to be set free.

BRUMPT (p. 772), on the other hand, points out the advantages of sternal puncture over spleen puncture in the diagnosis of kala azar: it is easy and almost painless; it is not dangerous and can be frequently repeated; the cell picture gives information of value in prognosis. In kala azar he found the average myelogram picture to be:—granulocytes 23 per cent., erythroblasts 24, hyaline leucocytes 53 per cent. Normally the granulocytes are 4 times as numerous as the erythroblasts and 3·5 times as numerous as the hyaline leucocytes. POPOTAS (p. 772) in Greece also writes of the value of sternal puncture, which he has used with success when spleen puncture and serum reactions were negative. REDDY and SUBRAMANIAM (p. 349), however, consider that negative sternal puncture does not exclude a diagnosis of kala azar. MATTEI *et al.* (p. 349) record a case of adult kala azar in

Corsica (where only the infantile form is commonly reported) which was diagnosed by the finding of leishmania in sternal puncture material. Serological tests were also positive.

HUANG (p. 773) describes a series of cases of agranulocytosis with sudden fall in the number of granulocytes, and with throat or skin lesions. In some the cause was kala azar, in others the condition was due to antimony treatment; the condition due to antimony appears to be more severe than that due to kala azar. Neostibosan and urea stibamine were the drugs responsible and it is suggested that antimony intoxication induces a sudden change in the number of granulocytes and that this favours the development of the acute condition. A platelet count of over 100,000 appears to be a favourable sign, and for treatment the drug of choice is pentnucleotide. Relapse may occur in the kala azar cases, so that antimony treatment should be resumed as soon as possible to prevent such recurrences.

WANG (p. 773) reports from China a case in which subcutaneous nodules, consisting of reticulo-endothelial cells and lymphocytes, with many leishmania, were found. A large amount of urea stibamine was needed in treatment.

Treatment.

In children undergoing treatment with tartar emetic for kala azar, VECCHIO (p. 350) noted that soon after the drug was commenced there was an increase in the lymphocytes of the blood, with a decrease in the neutrophiles and red cells. Bilirubinaemia was increased and reticulocytes became more numerous. These changes quickly passed off.

ROGERS (p. 350) states that with neostibosan and solustibosan a cure rate of over 90 per cent. can be expected in India, but that these drugs are too expensive for the villagers. If a cheap and efficient drug were produced and used on a large scale, kala azar in India could be reduced to small proportions. SUN (p. 775) also shows that in China the successful treatment of kala azar is related to the cost of the pentavalent antimony compounds. A new drug named Distibinyl has been prepared and is apparently as efficacious as other preparations but is cheaper. Details of dosage are given.

BHATTACHARJEE (p. 774) refers to alarming symptoms of an anaphylactic character which sometimes appear after the injection of pentavalent antimony compounds. These can be diminished by slow injection, using drugs, which are not too old, dissolved in double-distilled water and by keeping the patient lying down for half an hour after administration. Adrenalin, ephedrine or pituitrin may be given if the reactions are severe.

HORGAN and KIRK (p. 774), referring to the paper by ROGERS, point out the important fact that although antimony is highly successful in India, China and the Mediterranean, this is by no means true in the Sudan, where relapses after such treatment occur in a considerable proportion of cases. When relapse occurs there appears to be considerable resistance to further antimony treatment, so that the majority of relapse cases terminate fatally. [In this connexion later work indicates that 4 : 4′-diamidino stilbene is successful in the treatment of kala azar in the Sudan. It may be that this drug is effective in antimony resistant cases. See this *Bulletin*, 1941, Vol. 38, p. 261.]

ADAMS and YORKE (p. 775) report cure by 4 : 4′-diamidino stilbene of an Indian, with 8 intravenous doses of 1·0 mgm. per kilo., repeated daily. A total of 360 mgm. was given. ADLER and RACHMILEWITZ (p. 776) report a case of Mediterranean kala azar, in which there was relapse after a course of stibamine, which was treated with 4 : 4′-diamidino stilbene with apparently excellent results. Intravenous doses of 60 to 100 mgm. and intramuscular doses of 100 mgm. were given. ADLER and TCHERNOMORETZ (p. 775) write of the marked curative effect of 4 : 4′-diamidino stilbene in kala azar of hamsters. Doses of 2·5 to 40 mgm. per kilo. were given repeatedly.

CUTANEOUS (ORIENTAL SORE).

Oriental sore has been reported from the Southern Oranais district of Algeria and from Philippeville on the Mediterranean coast (RAMES, GUIGON, p. 351).

DUBOVSKOJ (p. 351) has cultivated *L. tropica* directly from human sores in Bianchi's medium, which is described. Incubation is at 20–22°C. SENEKJI (p. 351) describes the standardization of saline suspensions of culture forms of leishmania. He notes the biochemical reactions of *L. tropica* in cultures. He (p. 779) has tested the effects of various drugs on the flagellate forms of *L. tropica* in cultures. Trypaflavin, euflavin, rivanol and the green and violet dyes are the most actively lethal, but sulphanilamide has little action.

FLARER (p. 776) concludes, as a result of observations on smear preparations from oriental sore, that true schizogony takes place in the reproduction of leishmania, though he admits that the normal process is one of binary fission. In comment, WENYON points out that in making smears the cells containing the parasites suffer damage, and that small portions of broken-off cytoplasm containing a small number of parasites may easily give the impression of multinuclear forms. Reliable conclusions cannot therefore be drawn from smears, and it would be safer to study tissue sections.

VANNI (p. 352) found one specimen of *Phlebotomus macedonicus* infected in nature with leptomonads (probably developmental forms of leishmania) in the Abruzzi district of Italy, by the method of serial sections; in all, 1,600 were thus examined. Infection was also found in a batch of 200 flies which were ground up and injected into rats. He considers this sandfly to be the vector in this area. On the Adriatic coast of Italy he (p. 779) finds a definite association between oriental sore and *P. perfiliewi* (*P. macedonicus*) and there is little doubt that this sandfly is the vector. It breeds in dung heaps and it seems that the incidence of the disease is in direct relationship to the proximity of these heaps to the human habitations. In one province dung heaps are prohibited within 80–100 metres of houses, and oriental sore is practically non-existent, though the vector is present. Prevention, therefore, should include removal of dung heaps from the vicinity of houses, as well as protection by nets, treatment and education.

TRIFILÒ (p. 777) reports an oriental sore on the tongue of a patient in Eritrea.

BERLIN (p. 777) describes a condition in which, in the scar tissue of healed oriental sore there appear small round papules, resembling lupus vulgaris. In some of these leishmania have been found, probably enclosed in scar tissue during the healing of the original sore. These papules produce no symptoms and disappear spontaneously, leaving

varioliform scars. In one case papules also appeared on the extremities, away from the original sore. These were probably due to leishmaniasis, though leishmania could not be found in them.

AKRAWI (p. 779) treats oriental sore in Baghdad by local applications of M. & B. 693 or Uleron, and reports 63 per cent. of cures within a month, with good scar formation. This result is claimed to be better than those obtained with other forms of treatment.

MUCO-CUTANEOUS (AMERICAN).

VILLELA (p. 352) has found mucosal leishmaniasis to be about nine times as common in men as in women in São Paulo. In a large proportion the lesions are limited to the nasal mucosa and in many instances these lesions appear after skin lesions have healed. In some cases the nasal lesions develop before the skin lesions, and this would indicate that sandflies may feed inside the nose, a habit which has so far never been recorded. On the other hand it may be that the nasal condition is secondary to some latent skin infection which is not detected until the nasal lesion has developed. VILLELA *et al.* (p. 353) have found leishmania in scrapings from the apparently normal nasal mucosa of patients with cutaneous leishmaniasis in Brazil. This deposit of leishmania may probably lead to nasal lesions, and the treatment of cutaneous disease should include intravenous antimonials which are capable of destroying parasites in the nasal mucosa. The usual treatment of skin lesions with arsphenamine is not enough to eradicate the nasal infection.

PESTANO and PESSÔA (p. 776) describe cutaneous leishmaniasis from São Paulo and point out that the disease is associated with distinct monocytosis.

GOMES (p. 778) found the intradermal reaction of Montenegro to be strongly or moderately positive in 97·5 per cent. and weakly positive in 2·5 per cent. of cases of S. American cutaneous or muco-cutaneous leishmaniasis. The antigen used is a suspension of washed flagellates in physiological saline, containing 0·4 per cent. phenol. The antigen can be kept for long periods in the ice box with little loss of potency. *Charles Wilcocks.*

TRYPANOSOMIASIS.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

SALEUN (p. 304) shows that in French Equatorial Africa during 1939, the percentage of new native cases discovered in an early stage of the disease was 39·1 ; the percentage of cases in the nervous stage was 60·9. The various methods of examination, which are set out in detail, are complementary, and reliance should not be placed on one

method only; bone marrow puncture cannot replace the older methods. Treatment was much more effective in the early than in the late cases. Details are given of the present condition of patients treated up to 10 years ago. The author concludes that if immunity is provoked, it is of short duration only.

HAWKING (p. 306) has confirmed the finding of YORKE *et al.* that *T. rhodesiense*, as it occurs in the original host, is resistant to human serum, but that it becomes sensitive on passage through laboratory animals.

TEESDALE (p. 306) has found the proportion of fertile female *G. palpalis* to be found equal in blocks of riverine bush in Kenya, in spite of the fact that the fly density in these blocks, though low, is not equal. There is, therefore, no evidence that the remaining fly population is likely to die out of its own accord when reduced to a low level, since there is no indication that males and females are finding difficulty in meeting. In a study of *Glossina morsitans* in Tanganyika Territory, JACKSON (p. 307) has found that the flies are confined by the vegetational types to certain ambits, and do not usually stray from them. The length of life of male flies was studied, it is longest in the rainy season, since many die of starvation in the dry season when frequent feeds are necessary. Females move more extensively through the savannah than males, and probably live longer. JACK (p. 307) has discussed the behaviour in the field of *G. pallidipes* and *G. brevipalpis*, comparing these flies with *G. morsitans*. The findings cannot well be further abstracted, but include remarks on feeding preferences, results of trapping, state of hunger at the time of death, and the effects of humidity and heat.

BOWESMAN (p. 310) reports on 4 : 4′-diamidino stilbene in treatment in the Gambia. On intravenous injection there may be somewhat alarming symptoms which, however, soon pass off. The drug may also be given intramuscularly, a useful point in the treatment of children. It produces rapid amelioration of the symptoms and signs of sleeping sickness but is not suitable in cases in which the protein content of the cerebrospinal fluid is above 0·05 per cent. The treatment can be carried out in half the time necessary for tryparsamide; eye symptoms and albuminuria are not produced.

After observing for two years patients treated with neocryl. ACRES (p. 311) concludes that in an early stage of the disease this drug compares favourably with tryponarsyl, but in the later stages is much inferior to it.

HAWKING (p. 312) has investigated the trypanocidal activity and arsenic content of human blood and cerebrospinal fluid after the administration of tryparsamide.

FRANKS and FISHER (p. 313) report two cases of dermatitis which followed arsphenamine treatment and which recurred (an unusual happening) on the institution of tryparsamide therapy.

CULBERTSON (p. 314) has found that mother rats immunized by the injection of a formolized suspension of *T. lewisi* transmit their immunity to their young through the milk, as in the case of rats which have recovered from a *T. lewisi* infection. Any immunity acquired by the young through the placenta is largely lost within a few days after birth.

HOARE (p. 314) shows that in trypanosomes the kinetoplast may be absent without impairment of the vital functions. The akinetoplastic condition may be interpreted as a mutation depending upon

changes in the chromosome constitution, or as cytoplasmic inheritance, independent of the nucleus. He details the conditions under which absence of the kinetoplast may be found.

Chagas's disease.—MAZZA (p. 315) gives a list of animals found infected with *T. cruzi* in nature in certain provinces of the Argentine.

MAZZA and FREIRE (p. 316) report two cases of "inoculation chagoma" and describe the biopsy findings. MAZZA and URCELAY (p. 316) describe a further inoculation chagoma and a morbilliform rash in a child, and enumerate other skin lesions found in Chagas's disease. MAZZA and MIYARA (p. 317) also describe the same condition (without the rash) in an adult; stained biopsy specimens revealed leishmanial forms of *T. cruzi*. MAZZA *et al.* (p. 317) describe a child with secondary chagomata which were widely distributed over the body. As in one of the other cases reported, the preparation Bayer 7602 appeared to cause rapid improvement. MAZZA *et al.* (p. 318) describe the pathological histology of the chagomata which result from the cutaneous inoculation of *T. cruzi*, and refer to six cases in children and one in an adult. Several of these patients showed great improvement after treatment with the preparation Bayer 7602.

MAZZA and JÖRG (p. 318) have produced in a dog nodules indistinguishable from those of Chagas's disease by the injection of products of disintegrated *T. cruzi*. These products had been filtered through a Berkefeld V filter, and were capable of producing the Shwartzman phenomenon. *C. W.*

COOK (Albert). **How Sleeping Sickness came to Uganda.**—*East. African Med. Jl.* 1941. Jan. Vol. 17. No. 10. pp. 408–413.

In this address the author gives an interesting popular account of the history of sleeping sickness in Uganda. It contains nothing new. *W. Yorke.*

BRAZZAVILLE: AFRIQUE EQUATORIALE FRANÇAISE. RAPPORT SUR LE FONCTIONNEMENT DE L'INSTITUT PASTEUR DE BRAZZAVILLE PENDANT L'ANNÉE 1939 [SALEUN (G.)]. pp. 75–97.—Service de la surveillance de la maladie du sommeil. [**Sleeping Sickness Service.**]

During the year 1939 only a single case of sleeping sickness was found among the 438 Europeans examined. The number of new native cases discovered was 215; in addition, 645 old cases have been kept under observation, and of these 160 were discovered more than 10 years previously, 126 more than 5 years previously, and 359 less than 5 years previously.

Fifteen old European cases have remained under observation and all have enjoyed excellent health; details are given regarding the new case discovered during the year.

Information is given regarding the origin and condition of the 215 new native cases; 39·1 per cent. [wrongly given as 39·7] were in an early stage of the disease and 60·9 per cent. were in the nervous stage. These cases were discovered either by itinerant missions or because they had come to dispensaries with suspicious signs. In all 10,090

natives were examined for sleeping sickness during the year. The following table shows the method of examination which resulted in the discovery of trypanosomes :—

Presence of parasite.	No. of positive cases.
Gland juice alone	51
Thick blood film alone	1
Thick blood film + triple centrifugation	8
Gland juice + lumbar puncture	19
Thick blood film + lumbar puncture	1
Thick blood film + triple centrifugation + lumbar puncture	5
Gland juice + thick film + triple centrifugation	55
Gland juice + thick film + triple centrifugation + lumbar puncture	32
Lumbar puncture alone	43
	215

The various methods of examination are hence complementary, and it would be futile to rely on one only. The relatively large number of cases discovered by lumbar puncture when all other methods of examination had failed is worthy of note.

Among the 84 new cases in the first stage of the disease, treatment resulted in 72 blood sterilizations, 5 blood relapses, 3 nervous evolutions and 4 deaths ; among the 131 with nervous signs and changes in the spinal fluid, treatment gave good results in only 70 with return of the spinal fluid to normal.

The 160 cases discovered more than 10 years previously were all negative when re-examined during 1939. Of the 952 patients diagnosed between 1929 and 1933, 126 were re-examined during the year in question and 115 were found to be definitely cured, 9 to exhibit evidence of nervous evolution necessitating further treatment, and 2 to be infected. These 2 cases were undoubtedly re-infections, as frequent examination in previous years had shown them to be cured. Of the 970 cases diagnosed between 1934 and 1938, 359 were re-examined in 1939, and 273 found to be cured, 7 to have blood relapses, 78 to show signs of nervous evolution, and 7 to have been certainly re-infected [but these add up to 365].

The question whether re-infection is common receives consideration, but it is for obvious reasons difficult of solution. The author concludes, however, that notwithstanding the fact that it is rarely proved, immunity either does not occur or if it does is not of long duration in a person recovered from a previous infection. Details are given regarding 29 fatal cases—12 recently discovered during 1939 and 17 amongst old cases.

The last portion of the paper is concerned with the value of bone marrow puncture as a diagnostic measure [this *Bulletin*, 1939, Vol. 36, pp. 216–217]. Of 6 patients with peripheral infection 3 showed trypanosomes in the bone marrow, of 7 patients in the stage of meningeal reaction 5 showed a positive bone marrow, and of 4 in the nervous stage 3 had a positive bone marrow. Thus, of 17 cases shown to be positive by the ordinary methods 11 (65 per cent.) were found to be

positive by bone marrow puncture. Obviously then, this measure cannot replace the older methods of diagnosis and must be reserved for special cases. *W. Y.*

DUREN (A.). La lutte contre la maladie du sommeil au Congo Belge et au Ruanda-Urundi. [**The Fight against Sleeping Sickness in the Belgian Congo and Ruanda-Urundi.**]—*Rev. pour l'Etude des Calamités.* 1940. May–Dec. Vol. 3. Nos. 10–11. pp. 157–163. With 1 map.

This short article gives a semi-popular account of the disease and of the methods of combating it. In two interesting tables are shown the number of people examined, the number of old cases still under treatment, and the index of new infection for each year between 1928 and 1937 in the Belgian Congo and Ruanda-Urundi respectively. The general conclusion is that although sleeping sickness which is not combated is a calamity, this is not the case if the disease is attacked energetically. *W. Y.*

HAWKING (Frank). **Serum Resistance of** *Trypanosoma rhodesiense* **taken directly from Human Blood.**—*Jl. Trop. Med. & Hyg.* 1940. Nov. 1. Vol. 43. No. 21. pp. 255–257.

This note describes the resistance to human serum of two strains of *Trypanosoma rhodesiense* observed in their original host (man), and in subsequent passages through rats. When examined *in vitro*, these trypanosomes were wholly or partially resistant to serum taken from the patients or from a normal individual. This resistance was lost on passage of the strains through rats. These observations confirm the views of YORKE, ADAMS and MURGATROYD [this *Bulletin*, 1930, Vol. 27, p. 804] that the trypanosomes of *rhodesiense* sleeping sickness, as they occur in the original host, are resistant to human serum, but that they become sensitive on passage through laboratory animals.

Hawking notes that the trypanocidal activity of the serum of one of his patients was equal to that of a normal individual. The activity of the serum of the other patient seemed somewhat less. *W. Y.*

TEESDALE (C.). **Fertilization in the Tsetse Fly,** *Glossina palpalis,* **in a Population of Low Density.**—*Jl. Animal Ecology.* 1940. May. Vol. 9. No. 1. pp. 24–26.

This paper deals with the question whether, when the great majority of tsetse have been removed from an area, the small number left will increase and re-populate the district, or whether the fly will die out.

Glossina palpalis was formerly very common in the riverine bush on the Kuja river and its tributaries in the South Kavirondo district of the Nyanza Province, Kenya, but it has been practically eliminated over much of this area. The density of the fly, as measured by fly rounds, has been reduced from 100 to 200 tsetse per fly-boy-day to about 1 per F.B.D. This result has been obtained by using the "Block" method. The riverine bush has been divided into blocks up to several miles long by making clearings of about 1,000 yards wide, in each block the flies have been almost eliminated by hand-catching, squads of catchers having patrolled the blocks regularly and caught enormous numbers of tsetse.

It was suggested by K. MELLANBY that some idea of whether a sparse population of tsetse is likely to maintain itself may be obtained

by examining the spermathecae of the females captured. Flies caught in the six blocks on the Kuja river or its tributaries were examined. At first all females caught were dissected, but later it was found impossible to do this, and 1,737 out of a total of 2,956 females were examined.

The results of the dissections are summarized in a table, which shows that the percentage of infertile females is approximately the same in each of the six blocks, there being no evidence that a higher percentage of infertile females was to be found in the more sparsely populated areas.

The following summary is given :—

" Even when a population of the tsetse fly, *Glossina palpalis*, has been reduced to a low level, there is no indication that the males and females are finding difficulty in meeting. There is therefore no evidence that the remaining tsetse population is likely to die out of its own accord."

W. Y.

JACKSON (C. H. N.). **The Analysis of a Tsetse-Fly Population.**—*Ann. Eugenics.* 1940. Dec. Vol. 10. Pt. 4. pp. 332–369. With 4 figs.

The author has continued his studies of populations of *Glossina morsitans* in Tanganyika Territory. Flies are caught within a square with a side of 4 miles (subdivided into smaller squares), marked according to the date of capture, liberated, and recaptured at intervals thereafter. From the recaptures it is possible to estimate population, death, emergence and migration. The careful statistical analysis needed to give reliable results is fully explained. Most of the captured flies are males, so that the conclusions relate almost entirely to these. It is shown that about one-quarter of the male flies within the 4 mile square leave the square each week. But the majority of these have returned a week later ; only about 3 per cent. are permanently lost each week. The explanation appears to be that the flies are confined by the vegetational types to certain " ambits " and only rarely do they stray from one ambit to another. In this way the male flies are generally prevented from moving more than about half a mile in one direction. The length of life of male flies ranges from 2–6 weeks (average 4 weeks) throughout the year, being longest in the rainy season. A few individuals will survive 8 or 12 weeks at any season. In the dry season many die of starvation, for at this time they need frequent feeds, and, death being due to chance, the expectation of life is approximately equal at any age. In the dry season (in an area where fire was excluded for a year) the population fell, because of a fall in the emergence rate ; it rose again during the rains when emergence became normal and life became longer. The females move more extensively through the savannah than the males ; they probably live longer. *V. B. Wigglesworth.*

JACK (Rupert W.). **Notes on the Behaviour of** *Glossina pallidipes* **and** *G. brevipalpis*, **and Some Comparisons with** *G. morsitans.*—*Bull. Entom. Res.* 1941. Jan. Vol. 31. Pt. 4. pp. 407–430. With 7 figs.

The author states that the serious situation created by the continued incursions of *Glossina pallidipes* and *G. brevipalpis* from

Moçambique Territory into the farming area of the Southern Melsetter district in Southern Rhodesia has necessitated increased attention to these species.

Notes of interest on behaviour in the field, more especially of *G. pallidipes*, have been obtained, thanks to the courtesy of the Governor of Moçambique, who granted permission to Rhodesian entomologists to carry out investigations on the Portuguese side of the frontier. The area examined was the tract of country through which the motor road runs from Mt. Selinda in Rhodesia, past Spungaberra to the Gogoio Mission some 20 miles over the Portuguese border.

The author gives the following summary of the interesting observations recorded in this lengthy paper :—

" 1. *G. pallidipes* almost invariably attacks man on the leg from the knee downwards.

" 2. *G. brevipalpis* may attack man anywhere and not infrequently on the head.

" 3. Both species fill themselves readily with human blood once an attack has been made.

" 4. Neither sex of either species attacks man unless very hungry, as indicated by the very low mean fat content in the captures.

" 5. *G. brevipalpis* is apparently more reluctant even than *pallidipes* to attack man, and the fat contents in flies caught on man are proportionally lower than in the case of *pallidipes*.

" 6. Neither sex of *pallidipes* is attracted to a donkey unless hungry, *i.e.* ready to feed.

" 7. Male *brevipalpis* are apparently attracted to a donkey whether hungry or otherwise, but the females only when hungry. In this respect *brevipalpis* appears to resemble *morsitans*.

" 8. Both *brevipalpis* and *pallidipes* are very weakly attracted to a moving motor vehicle compared with *morsitans*.

" 9. It appears that males of both *brevipalpis* and *pallidipes* may be attracted to a moving motor vehicle when moderately fat, but the position in regard to the females is uncertain.

" 10. A grey blanket screen carried between two natives attracted *pallidipes* moderately and *brevipalpis* poorly.

" 11. *G. pallidipes* of either sex almost invariably settled on the bottom edge of the screen, whilst *brevipalpis* alighted anywhere on the side, and not infrequently on the top bar, level with the shoulders of the bearers.

" 12. The mean weight of fat in male *pallidipes* caught on the screen was rather lower than in the case of males caught on a donkey. In the case of the females, the mean weight of fat was the same in respect of both attractants.

" 13. Traps, more or less of the Harris type, but frequently with black cloth in place of hessian, caught a large number of *pallidipes* but very few *brevipalpis*.

" 14. Analysis of large numbers of trapped *pallidipes* revealed the fact that the mean fat content of the males was low, while the mean fat content of the females was much higher than in the case of females caught by means of any other attractant.

" 15. Of the trapped female *pallidipes* 14·5 per cent. were in advanced pregnancy, as against only 2·4 per cent. in the case of females of this species caught on a donkey.

" 16. The proportion of female *pallidipes* caught in the trap was 61·20 per cent. (2,430 flies).

" 17. In the case of the few *brevipalpis* caught in the traps the returns of fat also averaged high in the females and low in the males, but the numbers were too small for any reliable deductions.

" 18. It was judged from general observations that most *pallidipes* entered the traps between 4 p.m. and 5.30 p.m., dependent, however, upon the weather.

" 19. The most effective positions for the traps appeared to include those in which they received the rays of the sun in the later afternoon.

" 20. Further collections of *brevipalpis* males off the road in the late evening confirmed the fact that such males are mostly recently fed and fat.

" 21. Comparative tables are given showing the dry weight, weight of fat and stage of pregnancy in groups of *pallidipes* caught by means of different attractants.

" 22. It is probable that in the tables in the previous paper on *morsitans* many small 2nd stage larvae *in utero* were classed as 1st stage. The classification of 2nd and 3rd stage larvae in these tables refers to larvae 2 mm. or more in length, and the significance of the tables is not affected.

" 23. The figures given in Table XLIX in the paper on *morsitans*, which indicate a low proportion of 2nd and 3rd stage larvae in females caught on man, are of no significance as indicating reluctance of this sex to come to man. The last meal before larviposition appears normally to be taken when the larva is in the early 2nd stage.

" 24. The capture on a host of any considerable proportion of females containing advanced larvae does not indicate a thriving tsetse community, but betrays insufficient opportunity of feeding in the locality concerned.

" 25. Methods of estimating the state of hunger at the time of death in the case of dry tsetse flies are discussed.

" 26. Tables are given indicating the respective responses of *morsitans*, *pallidipes* and *brevipalpis* of both sexes to various attractants, and also, roughly, the proportion of the sexes in normal catches on these attractants.

" 27. It is remarked that no effective attractant for non-hungry *pallidipes* males has so far been found.

" 28. It is shown that there are certain consistent differences in the proportion between the mean weight of fat in the males and females respectively in catches of the different species on different attractants. If the female fat is expressed as percentage of the male fat the lowest figure refers to *morsitans* caught on man, whilst the highest refers to *pallidipes* caught in the traps.

" 29. Whilst in the case of both *morsitans* and *pallidipes* the traps tested have caught only lean (including young) males, but females in all stages of nourishment, young females seem to be inadequately represented in the catches of both species.

" 30. Figures obtained with *morsitans* indicate that the failure of the fat males and young females to be caught is due less to failure to be attracted to the outside of the traps than to failure to enter.

" 31. Under humid conditions relatively few lean *pallidipes* females of any age were caught in the traps, whereas under hot dry conditions old lean *morsitans* females were caught in considerable proportion. This is possibly due to the fact that in hot dry weather a low fat content is commonly associated with a reduced water content, but not necessarily in humid weather.

" 32. The figures indicating the alimentary condition of *pallidipes* caught in the traps are judged to support the view that hunger is not the primary stimulus leading to the attraction and capture of the flies.

" 33. In connection with the fact that only blood-sucking flies are caught in numbers in these traps, there are some indications that certain blood-sucking insects are more susceptible to heat than related vegetable feeders, but the question needs further investigation.

" 34. The fact that the traps catch flies only within a certain range of alimentary condition reduces their value as a barrier against fly movements.

" 35. The fact that well nourished heavily pregnant females are caught freely in traps erected in the open shows that such females must move about relatively freely.

"36. A cheap form of tsetse trap is described, and some notes on trapping results are included."

[See also this *Bulletin*, 1940, Vol. 37, pp. 400, 699.]

W. Y.

BOWESMAN (C.). **A Short Report on the Use of 4 : 4′-Diamidino Stilbene in the Treatment of Human Sleeping Sickness.**—*Ann. Trop. Med. & Parasit.* 1940. Dec. 31. Vol. 34. Nos. 3 & 4. pp. 217–222.

In this paper the author records his observations on the treatment of human trypanosomiasis in the Gambia with 4 : 4′-diamidino stilbene [this *Bulletin*, 1940, Vol. 37, p. 404.]. The drug was given intravenously, in doses of 1 mgm. per kilo. of body weight, twice weekly. The first set of cases were treated in hospital and were kept under very close observation, but later cases were treated as out-patients in country districts. Some of the patients received 7 injections and others 10.

Bowesman states that the drug, when administered by the intravenous route, is somewhat upsetting to the patient for the first two or three injections. Headache, sweating, tachycardia, vomiting or retching may occur, and there may be weakness of the pulse associated with a marked fall in blood pressure. The symptoms are of short duration and last only a few minutes, but they may be rather alarming at the time. Some of the patients fainted, but they recovered quickly. After the first three injections, however, only transient headache occurred. If the patient is cold before being treated, the symptoms are much more likely to be severe.

The following routine was carried out in all cases. After clinical diagnosis, blood examinations were made and these were followed by gland puncture and lumbar puncture. If these examinations confirmed the clinical diagnosis, treatment was begun. Before the second injection, blood examination and gland puncture were repeated, and if either was positive the examinations were again repeated before the third injection, and so on until negative results were obtained. After completion of the course of treatment, another lumbar puncture was performed, and possibly a final lumbar puncture was carried out one year after the course of treatment. Although in a large number of cases this final examination could not be carried out, clinical reports were received of almost all cases.

Detailed results are shown in a table. The cases are arranged in six groups: (*a*) those treated with 4 : 4′-diamidino stilbene with lumbar puncture performed before and after treatment and after an interval of a year; (*b*) those in which lumbar puncture was performed before and after treatment, but not a year later; (*c*) those in which the patients died before the course of treatment was completed; (*d*) those in which they relapsed or did badly and were subsequently given a course of tryparsamide; (*e*) control cases treated with tryparsamide alone; (*f*) control cases treated with Bayer 205 alone.

The following are the author's conclusions:—

"1. 4 : 4′-diamidino stilbene is a water-soluble drug suitable for intramuscular or intravenous injection in the treatment of early cases of trypanosomiasis in human beings.

"2. The drug can be given in doses up to 1 mgm. per kilo. body weight. Larger doses are not altogether safe by the intravenous route.

"3. Injection of the drug causes marked stimulation of the autonomic nervous system. The disturbance is temporary and no permanent harm results. The symptoms thus caused decrease with subsequent injections.

"4. There is a rapid amelioration in all symptoms of sleeping sickness, and physical signs improve quickly.

"5. Cases in which the cerebrospinal fluid protein is above 0·05 per cent. are not suitable for treatment with 4 : 4′-diamidino stilbene.

"6. No eye-symptoms were complained of during treatment.

"7. The drug does not cause albuminuria.

"8. Diamidino stilbene has an advantage over tryparsamide in the treatment of early cases of trypanosomiasis, as treatment can be carried out in half the time necessary for treatment with tryparsamide.

"9. When injected intramuscularly, the drug is not irritant and is very useful in the treatment of young children, where the veins are small and difficult to enter. Intramuscular tryparsamide is too irritant for the treatment of young children."

W. Y.

ACRES (Ian S.). **Further Observations on the Treatment of Sleeping Sickness with Neocryl.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1940. Nov. 30. Vol. 34. No. 3. pp. 281–289.

In this paper the author records later observations made on a number of cases of sleeping sickness treated with neocryl in 1936–37 [this *Bulletin*, 1938, Vol. 35, p. 341]. It has been found possible to examine most of the cases periodically within the last two years and thus to compare the value of the drug with that of tryponarsyl (tryparsamide). The dosage of neocryl corresponded closely with that used for tryponarsyl.

If, when the treatment with neocryl was completed, gland examination was negative and the cell-count of the cerebrospinal fluid normal, the patient was told to report for further examination after 6 months. If, however, the cell-count of the cerebrospinal fluid was raised or if there was any doubt about the clinical condition of the patient, he was told to report within a period of two or three months. If, on control examination, gland examination was still negative and the cell count of the cerebrospinal fluid normal, then a further period of 6 months elapsed before the next control was made. A case which showed no sign of relapse and was in good condition at least two years after treatment was completed, was considered cured. The results of this work are summarized in two tables, *viz.*, Table A showing (1) the controls of cases which were cured by neocryl, and (2) the earlier controls of those cases which relapsed after neocryl treatment; and Table B showing the further treatment and controls of cases which relapsed after neocryl treatment.

The cases are classified into groups, *viz.*:—

Group A.—First stage cases with weekly injections. Of 6 cases treated, 5 were apparently cured; one case relapsed.

Group B.—First stage with two injections weekly. Of 3 cases, one was cured and 2 showed definite signs and symptoms of relapse.

Group C.—Second stage with weekly injections. Of 10 cases, only 3 can be considered as cured, the other 7 showing definite signs and symptoms of relapse.

Group D.—Second stage cases with injections twice weekly. Both of the cases treated in this group relapsed.

Group E, which included cases previously treated with tryponarsyl before neocryl was used, has been disregarded. All the cases in this group have died.

It thus appears that of the 9 first stage cases treated with neocryl, 6 were cured and 3 relapsed, whilst of the 12 second stage cases, 3 were cured and 9 relapsed. These results are compared with those obtained during the same period by treatment with similar doses of tryponarsyl. Of 77 first stage cases treated with this drug, 69 were cured and of 67 second stage cases, 49 were cured. Acres considers that these figures show that the results obtained with neocryl in first stage cases on the whole compare favourably with those obtained with tryponarsyl, but in second stage cases neocryl treatment compares very unfavourably with that with tryponarsyl. *W. Y.*

HAWKING (Frank). **Trypanocidal Activity and Arsenic Content of Human Blood after Administration of Tryparsamide.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Jan. 31. Vol. 34. No. 4. pp. 305–310. With 1 graph.

This paper describes the trypanocidal activity produced in human plasma by the intravenous injection of tryparsamide. The methods used were similar to those employed by MURGATROYD, RUSSELL and YORKE [this *Bulletin*, 1935, Vol. 32, p. 26] in their experiments on rabbits.

The following summary is given :—

" 1. Persons were given an intravenous injection of tryparsamide and measurements were then made of the power of the plasma to kill trypanosomes of a serum-resistant strain of *T. gambiense*.

" 2. Immediately after the injection, trypanocidal activity was absent ; it rose to a maximum at 24 hours, at which time the minimum trypanocidal concentration (24 hours' exposure *in vitro* at 37°C.) varied between 1 : 2 and 1 : 8, corresponding to about 0·03γ per ml. of trivalent arsenic. The activity then gradually diminished and 4 days after the injection it was inappreciable.

" 3. Judging by a limited number of chemical estimations of the total arsenic content, tryparsamide disappears from the blood very rapidly after injection ; in two persons the arsenic content of the plasma, 24 hours after injection, was only 0·07 γ As. per ml.

" 4. The trypanocidal activity produced by tryparsamide in the blood was somewhat greater than that previously observed to occur in the cerebrospinal fluid, but its time relations were approximately similar.

" 5. Preliminary experiments indicated that neoarsphenamine produces a much greater activity in the blood than tryparsamide does, the minimum trypanocidal concentration of the plasma one hour after injection being about 1 : 1,000 (corresponding to 7 to 10γ per ml. of trivalent arsenic) ; after 24 hours this activity diminishes, so that it corresponds to 0·6γ As. per ml. These results confirm those obtained by MURGATROYD, RUSSELL and YORKE, working with rabbits."

W. Y.

HAWKING (Frank). **Trypanocidal Activity and Arsenic Content of the Cerebrospinal Fluid of Sleeping-Sickness Patients, after the Administration of Tryparsamide.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1940. Nov. 30. Vol. 34. No. 3. pp. 269–280. With 3 graphs. [10 refs.]

In previous papers (1937 and 1938) the trypanocidal activity and arsenic content of the cerebrospinal fluid of patients (mostly suffering

from general paralysis) in a mental home were examined after the administration of tryparsamide. In these cases the meningeal lesions, as shown by the cells and protein in the cerebrospinal fluid, were slight or absent.

In the present work these investigations were repeated on cases of human trypanosomiasis showing definite abnormality of the cerebrospinal fluid. The following are the conclusions :—

" 1. In previous papers, a method was described for the investigation of the trypanocidal activity *in vitro*, and of the total arsenic content of human cerebrospinal fluid, after the administration of tryparsamide ; these observations were made on patients in a British mental hospital with approximately normal cerebral membranes.

" 2. In the present work, similar observations were made on patients suffering from *rhodesiense* sleeping-sickness involving the cerebral membranes.

" 3. The average degree of trypanocidal activity observed in the cerebrospinal fluid after the intravenous injection of tryparsamide (3 grammes per 70 kg.) corresponded to 0·014γ per ml. at 17 hours, 0·01γ per ml. at 42 hours, 0·022γ per ml. at 65 hours, and 0·006γ per ml. at 96 hours ; it was inappreciable after 144 hours. The average total arsenic content of the fluid was 0·41γ per ml. after 17 hours, 0·12γ per ml. after 42 hours, and only slight traces after 65 and 96 hours.

" 4. These quantities are approximately similar to those observed in the series studied in Great Britain ; so that conclusions as to the relative merits of different arsenical compounds, reached by this technique in Great Britain, are applicable also when the same compounds are used for the treatment of sleeping sickness in Africa.

" 5. Apparently the occurrence of trypanosomal lesions of the cerebral membranes, as indicated by the increase of cells and protein in the cerebrospinal fluid, has no constant influence upon the penetration of tryparsamide into the fluid or on its activation therein.

" 6. The degree of trypanocidal activity produced by tryparsamide in the fluid of these patients is insufficient to exert much effect upon freshly isolated strains of *T. rhodesiense*.

" 7. When patients were treated with neocryl or with undecane diamidine, only insignificant degrees of trypanocidal activity were produced in the cerebrospinal fluid."

W. Y.

FRANKS (Andrew G.) & FISHER (Samuel). **Sensitization to Arsenical Compounds. Sensitization to a Pentavalent Arsenical following Use of a Trivalent Arsenical.**—*Arch. Dermat. & Syph.* 1940. Nov. Vol. 42. No. 5. pp. 808–810.

The authors state that in a review of the literature on sensitivity to arsenical drugs they found only three cases of sensitivity to both trivalent and pentavalent arsenicals (EPSTEIN, 1937 and GOLZ, 1939). In all the three cases an exfoliative dermatitis developed on the administration of neoarsphenamine and the eruption recurred after injections of tryparsamide.

Details are given of two further cases of arsenical dermatitis following neoarsphenamine therapy. Recurrence of the dermatitis took place on the institution of tryparsamide therapy. *W. Y.*

CULBERTSON (James T.). **Natural Transmission of Immunity against *Trypanosoma lewisi* from Vaccinated Mother Rats to their Young.**—*Jl. Parasitology.* 1941. Feb. Vol. 27. No. 1. pp. 75–79.

Previous work [this *Bulletin*, 1939, Vol. 36, p. 751] has shown that mother rats and mice, after recovery from trypanosome infections, transmit specific protective substances to their young. These substances are presumably identical with the antibody of the serum, and they are passed to the young largely or entirely through the milk of the mother, and only in small amount, if at all, through the placenta.

In the present work the author has investigated whether mother animals, immunized not by infection but by vaccination with a formolized suspension of trypanosomes, likewise transmit protective substances to the young in an amount sufficient to protect the young from the specific infection. The parasite employed was *Trypanosoma lewisi*, and the vaccine was prepared as follows: rats 15 days old when infected with *T. lewisi* were bled from the carotid when their infections were near the peak. The citrated blood was slowly centrifuged in order to separate the trypanosomes, which were then suspended in 0·5 per cent. formolized physiological sodium chloride solution, and their number determined by counting with a haemocytometer. For injection, a suspension containing 4·3 million organisms per cubic centimetre of fluid was employed.

Results of the experiments, which are given in detail, show that mother rats immunized against *T. lewisi* by vaccination in this way transmit their immunity to their young. The young become immune largely by ingesting the milk of the immune mother. Such immunity as the young may acquire through the placental circulation is largely lost within a few days after birth. *W. Y.*

HOARE (Cecil A.). **Recent Studies on the Kinetoplast in Relation to Heritable Variation in Trypanosomes.**—Reprinted from *Jl. Roy. Microscopical Soc.* 1940. Vol. 60. pp. 26–35. With 3 figs. [32 refs.]

Although the kinetoplast is typically a permanent structure in trypanosomes, it may be absent in some or all individuals of certain strains or races under certain conditions. As in trypanosomes devoid of kinetoplasts all the vital functions remain unimpaired, it is clear that this structure—whatever its physiological rôle may be—is not indispensable for the existence of the flagellates.

The production of strains devoid of the kinetoplast presents an interesting problem in the genetics of trypanosomes, and consequently the various ways in which this may happen are considered:—

1. *Individual variation.*—In strains of different species of trypanosomes a certain proportion of individuals lack the kinetoplast, *e.g.*, in typical strains of *T. evansi* akinetoplastic trypanosomes may vary from 0 to 8 per cent., this proportion fluctuating further within the same population at different periods of the infection.

2. *Induced disappearance.*—Totally akinetoplastic strains may be produced by treating with certain dyes. Such strains remain akinetoplastic indefinitely. The action of the dyestuff appears to be twofold; it may destroy the kinetoplast directly or cause it to disappear, or it may deprive it of the power to divide, with the result

that when the trypanosome divides it gives rise to one daughter individual with a kinetoplast and to one without this structure.

3. *Spontaneous disappearance.*—*T. equinum* is in nature the only strain of trypanosomes totally devoid of a kinetoplast, and it is thought that it might have originated from *T. evansi* through the loss of this structure. Recent observations have thrown further light on this problem. A normal strain of *T. evansi* maintained in the laboratory for 5 years suddenly became akinetoplastic (WENYON, 1928, etc.); and Hoare and BENNETT (1937 and 1939), who examined the blood of more than 100 camels, from the Anglo-Egyptian Sudan, infected with *T. evansi*, found that 5 of the strains were akinetoplastic. One of the latter was transferred to laboratory animals and for 3 years the aberrent condition has remained unchanged.

4. *Fluctuating variation.*—Another strain of *T. evansi* isolated from a camel at first exhibited 1 per cent. of akinetoplastic forms, but in subsequent passages through rodents the percentage underwent great fluctuations between a maximum of 71 and a minimum of 1.

The next portion of the paper is devoted to an analysis of the data from the point of view of genetics. It must be read in the original by those interested.

The following are the conclusions :—

"It has been shown that the akinetoplastic condition in trypanosomes can be interpreted either as *mutation*, depending upon changes in the chromosome constitution, or as *cytoplasmic inheritance*, independent of the nucleus. However, since many cases of plastid modification in plants are known where the change is controlled directly or indirectly ("maternal effect") by genes, it is possible that both types of inheritance actually belong to the same category and are determined by factors in the nucleus (*cf.* Dobzhansky, 1937; Sinott and Dunn, 1939).

"It is clear that the question regarding the genetic mechanism concerned with the origin and perpetuation of the akinetoplastic condition in trypanosomes stands in need of further investigation, and it is with the object of drawing attention to this interesting problem that the present review has been written."

W. Y.

MAZZA (Salvador). Investigaciones sobre enfermedad de Chagas. IX. Otros mamíferos infectados naturalmente por *Schizotrypanum cruzi*, o *cruzi* similes en provincias de Jujuy y Salta. [**Mammals found Naturally Infected by** *T. cruzi* **in Jujuy and Salta.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 45.* 1940. pp. 119–134. With 19 figs.

By examination of the blood in thick drop and by xenodiagnostic methods Professor Mazza has now shown that the following animals are naturally infected by *T. cruzi* in the provinces studied :—

In Jujuy: Mustelidae: *Tayra barbara*: Canidae: *Pseudalopex culpeus andinus*; Sciuridae: *Leptosciurus argentinus*; Cheiroptera: *Histiotus laephotis* (bat).

In Salta: Canidae: *Pseudalopex gracilis gracilis*; Cheiroptera: *Myotis dinellii, M. nigricans*; Edentata: *Chaetophractus vellerosus pannosus, Tolypeutes matacos, Histiotus montanus*; Marsupiales: *Didelphys paraguayensis.* *H. H. S.*

i. MAZZA (Salvador) & FREIRE (Ramon S.). Investigaciones sobre enfermedad de Chagas. Manifestaciones cutáneas (Chagomas). I. Manifestaciones cutáneas de inoculación, metastáticas y hematógenas en enfermedad de Chagas. Chagomas de inoculación, chagomas metastáticos y chagomas hematógenos. [**Manifestations of Chagas's Disease, Cutaneous from Inoculation, and Metastatic Haematogenous.**]—*Universidad Buenos Aires : Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 46.* 1940. pp. 3–38. With 45 figs.

ii. —— & ——. Investigaciones sobre enfermedad de Chagas. Manifestaciones cutáneas (Chagomas). II. Lipochagomas genianos por contigüidad y metastáticos. Lipochagomas genianos hematógenos. Su importancia diagnóstica en formas agudas de enfermedad de Chagas sin otras manifestaciones aparentes en lactantes.—*Ibid.* pp. 39–57. With 8 figs.

i. Two instances of local inoculation Chagoma, with secondary metastatic haematogenous tumours, are described in children aged 14 months and two years respectively, with photographs of the patients and photomicrographs of the histological changes found in tissue taken by biopsy. The children had complained of pain in certain regions and the parents had detected local swellings and consequently sought medical advice. The photographs are beautifully reproduced.

ii. A similar case calling for no detailed abstract. *H. H. S.*

MAZZA (Salvador) & URCELAY (Gilberto). Investigaciones sobre enfermedad de Chagas. Manifestaciones cutáneas (Chagomas). III. Caso de enfermedad de Chagas con chagoma de inoculación seguido a los 15 días de esbozo de complejo oftalmo-ganglionar y esquizotripanide morbiliforme. [**Chagas's Disease with Inoculation Chagoma followed by Morbilliform Exanthem.**]—*Universidad Buenos Aires : Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 46.* 1940. pp. 58–84. With 39 figs.

A very fully described case in a boy of 18 months. The article is embellished with a large number of photomicrographs showing the tissue changes. The "inoculation chagoma" was present on the anterior surface of the left thigh, and sections from tissue taken by biopsy on the 15th day of disease showed numerous leishmanial forms in the skin and the cytological steatonecrosis. The day of disease was counted from the onset of oedema of the eyelid (Romaña's sign) and conjunctival injection. Treatment with 7602 Bayer was speedily followed by disappearance of the ocular symptoms and fading of the morbilliform eruption.

The authors thus enumerate the cutaneous lesions of Chagas's disease :—

(1) Invasion of the skin itself ; (2) extension to the subcutaneous cellular tissue ; (3) Intense involvement of the epithelium with destruction and necrobiosis ; (4) inflammatory cytosteatonecrosis, with leishmanial forms of *T. cruzi* present in the fat cells ; (5) centripetal lymphangitis and nodular formations along the paths of the vessels ; (6) subepithelial infiltration with obliteration (borramiento) of the line of distinction of the epidermis and corium. *H. H. S.*

MAZZA (Salvador) & MIYARA (Salomon). Investigaciones sobre enfermedad de Chagas. Manifestaciones cutáneas (Chagomas). IV. Enfermedad de Chagas aguda con chagoma de inoculación y esquizotripanide polimorfa comprobado por histopatología de biopsia de la lesión cutánea. [**An Acute Case of Chagas's Disease with Chagomata.**]—*Universidad Buenos Aires: Misión de Estudios de Patologia Regional Argentina (Jujuy). Publicación No. 46.* 1940. pp. 85–104. With 27 figs.

This is another case of what has been described above, but calls for particular attention because it is probably the first time that diagnosis has been based upon biopsy of the "inoculation chagoma." The patient was a man of 41 years who complained that, about midnight on a certain occasion, he felt a sudden pain in his left arm and noticed a red painful spot, but no sign of a bite or puncture. The following morning he found near his bed a bug which had fed on blood. Five days later the left upper arm showed a rash of small spots (papules), followed by a circinate eruption of the chest and upper part of the abdomen, reddish in colour, disappearing on pressure. The eruption persisted for twelve days. Three weeks after his midnight experience he had oedema of the left eyelids, which lasted for one day, and a certain amount of pain in that eye continuing for ten days, although examination of the eye revealed no cause. Examination of his blood by thick drop and by xenodiagnostic methods proved negative, as did smears of tissue taken from the arm lesion. Stained sections, however, revealed leishmanial forms of *T. cruzi* and the histological changes recorded in the foregoing abstracts. *H. H. S.*

MAZZA (Salvador), BASSO (Germinal), BASSO (Redento) & CONTE (Donato). Investigaciones sobre enfermedad de Chagas. Manifestaciones cutáneas (Chagomas). V. Caso agudo de enfermedad de Chagas con chagoma de inoculación antibraquial, chagomas múltiples metastáticos y hematógenos y complejo oftalmoganglionar izquierdo. [**An Acute Case of Chagas's Disease with Inoculation and Metastatic Chagomata.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 46.* 1940. pp. 105–118. With 11 figs.

One more case, this time in a child of two years, recorded because of the wide distribution of secondary chagomata. The child's mother had noticed when it was first taken ill that there was a swelling of the eyelids of the left eye and a hard, dark coloured, prominent area, the size of a chestnut on the postero-internal aspect of the left forearm. Three weeks later several cutaneous swellings were observed by the mother, one over the left breast, two on the left flank. The child was brought to hospital and a thick drop of the blood revealed *T. cruzi* in fair numbers (five in a preparation). Two or three days later other swellings were seen: in the suprahyoid region, midline, the size of an olive, hard and adherent to the skin; the left pectoral region, 8 cm. in diameter, raised, red-violet, hard, "cartilaginous," adherent to the skin but moving over the deeper structures; the right pectoral region, $3 \times 2{\cdot}5$ cm. without discoloration and found by palpation; in the thoracic wall at the right axilla, hot and discoloured; others in the left axilla without modification of the overlying skin; in the left flank two, one as large as an orange, the other somewhat smaller

extending back to the lumbar region, the skin over them being hard and discoloured. All these are well shown in photographs. Improvement followed rapidly on the administration of 7602 Bayer, though in smaller doses than those recommended by Mazza, 90–120 mgm. per kilo. bodyweight. *H. H. S.*

MAZZA (Salvador), BASSO (Germinal) & BASSO (Redento). Investigaciones sobre enfermedad de Chagas. Comprobación, en adulto, de citoesteatonecrosis subcutánea chagásica por siembra hematógena (*Chagomas hematógenos*) de *S. cruzi*. [**A Case of Haematogenous Chagoma in an Adult.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 48.* 1940. 30 pp. With 25 figs. [10 refs.]

Chagoma is the name given to a tumour formation resulting from cutaneous inoculation of *T. cruzi* and it may be followed by metastatic swellings spread by the blood stream. Its characteristic pathological lesion is a fat necrosis of the tissue cells, especially the subcutaneous fat. This fatty necrosis is not a secondary degenerative change but part of the initial inflammatory stage of invasion, and is a manifestation of the colonization of the leishmania forms in the fatty tissue. Six cases are briefly referred to, in children ranging in age from three to twenty-one months [in one the age is not stated]. They showed the primary "inoculation chagoma" with secondaries 2–3 months later. Two of the six died; these had not received treatment by 7602 (Ac) Bayer; the others received it and recovered.

The author records in much detail an analogous case in a man of 50 years, who presented himself with 19 of these tumours, 18 of them discovered by palpation, another in the right axilla harder, firmer and more defined. At first the Machado reaction and inoculation experiments on puppies were negative, but later positive. A biopsy was made of the axillary swelling and the pathological histology is described in minute detail and depicted in an excellent series of photographs showing invasion of the dermis and the presence of the leishmanial stage of *T. cruzi* in the histiocytes of the tissue. The patient was given 5 cc. of 7602, intramuscularly [see this *Bulletin*, 1940, Vol. 37, p. 146]; this was repeated two days later and the swellings were much improved. Four days later he was given by injection 20 cc. of a 3 per cent. solution freshly prepared. The tumours then rapidly disappeared. In all he had 22·2 mgm. per kilogramme. *H. H. S.*

MAZZA (Salvador) & JÖRG (Miguel E.). Investigaciones sobre enfermedad de Chagas. Reproducción experimental de nódulos de histiocitosis del granuloma chagásico mediante el fenómeno Shwartzman. (Existencia de principio activo de *Schizotrypanum cruzi*, capaz de provocar hiperplasia histiocitaria y su confluencia plasmodial.) [**Histiocyte Nodules produced experimentally: *T. cruzi* and the Shwartzman Phenomenon.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 47.* 1940. 18 pp. With 11 figs.

From the intestinal contents of *Triatoma infestans* a strain of *T. cruzi* was obtained and cultivated. The contents of four tubes were emulsified in 40 cc. of sterile NaCl solution, 0·85 per cent., in a 100 cc.

flask containing 20 gm. of powdered glass. This was shaken for 6 hours, to disintegrate the bodies of the trypanosomes. The resulting emulsion was filtered through cotton, then paper and finally through a Berkefeld V. With the product the authors produced in a dog nodules of reticular histiocytes indistinguishable from the lesions of Chagas's disease in man and animals. Considering the mode of preparation of the substance we may say that the nodules are due to a water-soluble substance not dialysable; that there is in *T. cruzi* a specific substance which, evidenced by the Shwartzman phenomenon, can provoke reticular histiocytosis; it may be inferred that it is the destruction of the protozoon in inflammatory foci or in macrophages that give rise to the formation of these nodules in infected man or animals. The Shwartzman phenomenon is exhibited by primary local sensitization, giving rise to the characteristic phase of the phenomenon by injection of the same substance into the blood stream. One sees its parallel in natural infection—a primary local lesion, and a subsequent haematogenous dissemination with local excitation of foci already sensitized by parasitic action. *H. H. S.*

MAZZA (Salvador) & others. Investigaciones sobre enfermedad de Chagas. I–XI. [**Investigations on Chagas's Disease.**]—*Universidad Buenos Aires: Misión de Estudios de Patología Regional Argentina (Jujuy). Publicación No. 45.* 1940. 152 pp. With numerous illustrations.

This volume contains eleven papers, by Mazza and his colleagues, on Chagas's disease in the Argentine. The papers are concerned with clinical findings, studies on the vectors, and on mammalian hosts of *T. cruzi.* *C. W.*

PLAGUE.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

MOLL and O'LEARY (p. 321) write of the history and epidemiology of plague in the Americas. This work cannot be further summarized, but it is noted that in Bolivia, the last of the American countries to be invaded by the disease, man himself is believed to have played the principal part in transmission. This is ascribed to the practice of holding wakes over the dead, with a final partition among the visitors of the blankets and clothing belonging to the deceased. BARRETO (p. 322) reports on plague in Brazil. It has occurred in many cities ind there is a focus in the north-east. It is endemic in São Paulo. an Pernambuco the disease is largely rural in distribution; it increases In the harvest season and is affected by temperature and humidity. *Mus rattus* predominates in rural areas and *Xenopsylla cheopis* is the most prevalent flea in rural areas and in ports. A campaign against rodents and fleas has been initiated in the north-east, and vaccination has been used on a considerable scale; the best results were obtained with a vaccine prepared at room temperature.

JUNIOR (p. 323) refers to cultural differences between the motile *P. pestis* and the non-motile *P. pseudotuberculosis rodentium* [see

BHATNAGAR below]. In reporting on plague in São Paulo he remarks that a 2 per cent. rat plague infection presaged a local human epidemic. A flea index of only 3 per rat is scarcely compatible with the occurrence of human plague. Glands from suspected rats are sent from the interior in Broquet's solution, of which the composition is given.

In Mendoza DE LA BARRERA (p. 324) finds that sylvatic rodents have little contact with domestic rats, and that this accounts for the comparative absence of human plague in the presence of widespread epizootic. Sylvatic plague remains latent and although human cases are rare, its presence is undoubtedly to be regarded as a danger ; under conditions of great increase of the sylvatic fauna, as may happen with an abundant harvest of maize, the access of plague to man will be rendered easier.

In the western part of the United States, ESKEY and HAAS (p. 324) show that plague is widely spread in wild rodents but that this has not been accompanied by infection of domestic rats. Some 50 species of fleas infest wild rodents and may show a certain degree of specificity for their hosts, though this is not complete. Most infected fleas harbour the bacilli throughout their lives, and the life span, after a flea has transmitted plague for the first time, averages three days, with occasional survivals up to 11 days. There is, however, an incubation period in the flea before transmission is possible, and this may vary from 5 to 130 days. Plague does not damage the fleas until blockage occurs, when the flea dies of starvation. Since chloroform and ether are apt to destroy *P. pestis* they should not be used in the collection of fleas from rodents ; cyanide gas is better for this purpose. At refrigeration temperature *P. pestis* harboured by fleas may retain its virulence for 6 months or more. For transporting fleas to be used for inoculation a 2 per cent. salt solution is recommended ; this inhibits the growth of other bacteria. In detecting plague in wild rodents the importance of inoculating their fleas into test animals is emphasized. BYINGTON (p. 326) reports that epizootic outbreaks are occurring in rodents in the Western United States and that these are part of a widespread enzootic. No human cases are known to have been associated with the disease in rodents.

GIBBONS and HUMPHREYS (p. 326) report on plague surveys in Western Canada, which refer to rats, rat fleas and sylvatic plague rodents. It is not known how infection in wild rodents was introduced into Alberta but the potential hazards make it a matter of concern. It has not yet been found in British Columbia.

BHATNAGAR (p. 327) describes the envelope of the plague bacillus, which he distinguishes from a capsular structure such as is present in the pneumococcus. Strains of *P. pestis* may be virulent or avirulent, and the latter may be protective or non-protective for purposes of immunization. Virulent strains possess envelope substance in fairly large quantity, protective avirulent strains have less, and non-protective avirulent strains have no envelope substance but may acquire it if grown on horse serum agar. The largest amount of envelope substance is developed during growth at 37°C. He (p. 328) discusses the difficulty in distinguishing between *P. pestis* and *P. pseudotuberculosis rodentium* [see Junior, above]. He has found that certain strains of *P. pestis* possess envelope substance and that this interferes with the somatic type of agglutination. *P. pseudotuberculosis*, however, possesses no envelope substance but has a common somatic antigen with *P. pestis*. Suspensions made by mixing the two

organisms were used for agglutination tests of envelope and somatic antigens and for immunization of animals. The author remarks that, to obtain reliable results in the serology of plague and of pseudotuberculosis, living organisms should be used, but if killed suspensions are preferred, plague bacilli killed by chemicals and pseudotuberculosis organisms killed by heat should be employed.

BURTON and HENNESSEY (p. 329) report a case of meningitis due to plague.

BONEBAKKER (p. 329) considers that the serum treatment of plague is useful and that it should be given at an early stage. He gives the serum intravenously and, at the same time, in and around the bubo.

OTTEN (p. 330) sums up his experience with live vaccine. From early experimental work he came to the conclusion that it was impossible to obtain satisfactory immunity with a dead vaccine in the house rat and the guineapig. In working on the problem of live vaccines he isolated the Tjiwidej avirulent strain which could not be made virulent but which had high immunizing power. When this strain was used to immunize man in doses of one-fifth of an agar culture, the mortality over a large series of cases was only 20 per cent. of that in unvaccinated populations. In one area the deaths from plague were rapidly reduced to zero when this live vaccine was used on a large scale. The vaccine should be used as quickly as possible after preparation and modern dosage is 1/50th of an agar culture. *C. W.*

MOLL (Arístides A.) & O'LEARY (Shirley Baughman). **Plague in the Americas: an Historical and Quasi-Epidemiological Survey.**—*Bol. Oficina Sanitaria Panamericana.* 1940. May, June, Aug. & Sept. Vol. 19. Nos. 5, 6, 8 & 9. pp. 451–461; 576–584; 759–771; 878–887. With 1 map. [Refs. in footnotes.]

I. Many publications of the progress of plague in the Americas, north and south, have appeared in recent years. Some of these have dealt with separate States and some with the Republics of America, The present article deals particularly with Paraguay, Argentina. Brazil, Uruguay, Venezuela, Bolivia, Peru, Chile, Ecuador, The United States, Mexico, Panama, and The West Indies. These are valuable for reference purposes, but perhaps the most interesting observations relate to the exceptional and negative instances regarding plague infection. Thus "the last country in which plague has been recognized is Bolivia." Many States such as Colombia, the Guianas, Central America, the Dominican Republic and Haiti, together with some smaller islands have not yet been invaded and the explanation of this immunity is still unsatisfactory. In other States it has proved easy to eradicate plague; these are Cuba, Mexico, Porto Rico, Panama and Uruguay and again the reason is still to seek. It was to be expected that "sylvatic plague" would receive special mention. This type of plague has come to be established in the country districts where no rats are present and has served to keep infection going as a potentially grave danger after the difficult task of clearing the ports has been accomplished. A great contribution to the diagnosis of plague was made by America with the introduction of mass inoculation and the inoculation of pooled fleas as a first resort in determining the actual existence of rodent plague. Much valuable literature on plague has been contributed for many years by Latin American countries, some of it not as well known by English readers as it deserves to be.

Other subjects treated in this article relate to pneumonic and other types of plague, vaccines and sera, variations with season and altitude, rats and other carrier animals, fleas and lice. Pneumonic plague made an early appearance in the original outbreak in Asuncion in April 1899 and has a very high mortality. Although vaccination is more or less a routine measure, especially for plague personnel, there seems to have been no definite conclusion drawn as to its efficacy.

It is interesting to learn that : " Of the American countries invaded by plague, Mexico, the West Indies, Chile, Paraguay and Uruguay are now apparently free. All seaports are also free and the international danger is to-day considered comparatively slight," if due precautions are taken. A chronological outline of plague in the Americas from 1898 to 1939 concludes the article, the last sentence of which is : " 1939 December, 1 case human plague reported in United States (Utah), first human case since 1937."

II. *Argentina.*—Plague broke out in Argentina five months after the first cases in Asuncion. At first it was unrecognized and then discredited owing to the vigorous opposition to the diagnosis by authorities, the press and the public. In time this was remedied and antiplague measures are now highly efficient.

Investigations have been made into the rat and flea. plague vector question. It is interesting to note that while *X. cheopis* is the dominant plague flea foreign fleas have entered Argentina and the proportion of *X. cheopis* has fallen from 95 per cent. to 65 per cent. Rural plague was associated as far back as 1905 with the wild guineapigs of Argentina, the cuis. This was abundantly confirmed and it has been found that areas formerly abounding in cuis or *Graomys* have become entirely depopulated after an epizootic of plague. And yet human infection is rare, in spite of widespread epizootics.

Plague control measures have gone through all the usual phases from the date of entry of plague into any country. At the present time the procedure is essentially an anti-rat campaign, deratization in all its forms—rat killing, rat poisoning, rat trapping, rat proofing and so on.

III. *Bolivia.*—Bolivia has the distinction of being the last of the American countries to be invaded by plague, this immunity being due to its " isolated land-locked situation." Some special features have characterized plague in Bolivia, in particular : " Man himself is believed to have played the principal part in the transmission." This is ascribed to the practice of holding wakes over the dead with a final partition among the visitors of the blankets and clothing belonging to the deceased.

Plague control has proved very difficult, partly because of the poor living conditions and poor education of the people and partly because of the wooded, broken nature of the country. Plans for a permanent plague control campaign were drawn up in 1938. Sylvatic plague constitutes a major problem here as elsewhere throughout America.

W. F. Harvey.

BARRETO (João de Barros). O estado atual do problema da peste no Brasil. [**Plague in Brazil.**]—*Bol. Oficina Sanitaria Panamericana.* 1940. Sept. Vol. 19. No. 9. pp. 866–877. English summary.

" The ex-Director of the National Department of Health of Brazil analyses the plague situation in that country. In the southern ports and cities the last cases of plague reported were : Belém, 1912 ;

Fortaleza, 1936; Recife, 1924; Maceió, 1925; Salvador, 1928; Rio de Janeiro, 1928; Santos, 1931; Paranaguá, 1926; and Porto Alegre, 1933. A rather extensive focus in north-east Brazil (States of Piauí, Ceará, Paraíba, Pernambuco, Alagoas, and Baía) is described at length, and another one, less well known, in S. Paulo. In that city the disease is endemic, with human cases every year, a total of 66 having been reported from 1930 to 1939. In the north-eastern focus, 1,542 cases were observed from 1934 to 1939. The bubonic form has predominated in this area. With the exception of three cases observed in 1939 in certain towns in the State of Pernambuco, all the other cases of that year (75), and the 85 cases of the year 1938 occurred in rural districts. Plague increases in the harvest season: May to June in Ceará, August to November in Pernambuco. It is also affected by temperature and hydrometric conditions, since these influence the longevity and propagation of fleas and the fertility, number and aggressiveness of rats. *Mus rattus* predominates in the rural areas, constituting 90 per cent. of the rats caught in Ceará, 74 per cent. in Triunfo (Pernambuco), 90 per cent. in Princesa, and 62 per cent. in Campina Grande. The most prevalent flea is *X. cheopis*, with *X. brasiliensis* running second. *X. cheopis* is also the most prevalent flea in ports: 98 per cent. in Salvador, 85 per cent. in Fortaleza, 79 per cent. in Maceió and 60 per cent. in Recife. After a detailed study, and having trained the necessary personnel, the Federal Government in 1936 initiated an intensive anti-plague campaign throughout the entire north-east area, centering its attack on isolated foci. The campaign followed the general lines of combatting rodents and their parasites, in addition to the vaccination of susceptible individuals. Some 5,000 persons were vaccinated in 1937, about 27,000 in 1938, and almost 5,000 in 1939. At first the vaccine of the Oswaldo Cruz Institute was used (2 cc. of culture in glycerinated agar, submitted to 65°C. for an hour), but it was later found that better results were to be obtained from the vaccine of the Public Health Laboratory, prepared in peptone-gelose at room temperature. The success of the campaign is evidenced by the decrease in the number of cases from 208 in 1934, 822 in 1935 and 314 in 1936, to 35 in 1937, 85 in 1938, and 78 in 1939."

JUNIOR (F. Prado). O serviço de laboratório na profilaxia da peste em São Paulo. [**Plague Laboratory Service in São Paulo.**]—*Bol. Oficina Sanitaria Panamericana.* 1940. Oct. Vol. 19. No. 10. pp. 971–979. With 2 figs. on 1 plate.

Within a few days of the start of the Butantan Institute as plague prophylactic laboratory for São Paulo a focus of rat plague was discovered. Over 3,000 rats were killed and plague was stamped out. It is necessary, however, to be careful after such a campaign not to assume complete riddance of rodent plague, as the disease may remain latent for a considerable time. A diminution of the rat population by 50 to 75 per cent. should ensure 12 to 18 months of freedom from plague. The practice of the laboratory followed the usual lines of macroscopic and microscopic diagnosis and took special notice of the cultural differences between the non-motile *P. pestis* and the motile *P. pseudotuberculosis rodentium.* The various rat and flea indices were found to be most helpful. Thus a 2 per cent. rat plague infection presaged a local human epidemic. A reduction of the usual proportion of 4 to

5 female rats to 1 male indicated that the poison baits were effective for it is the female that is specially active in search of food. When the usual *R. norvegicus* proportional capture of 85 per cent. to the 15 per cent. of *R. rattus* and *alexandrinus* became lowered to 50 per cent. for *norvegicus*, it meant that the *norvegicus*, a ground rat, was being eliminated and that the other species, which are roof rats, were becoming relatively increased. With diminution of the rats the fleas diminish and the flea index is lowered. A flea index of only 3 per rat is scarcely compatible with the occurrence of human plague.

Lymph glands from suspected plague rats from the interior of the State were sent to the laboratory in Broquet's solution :—neutral glycerine 20 ; calc. carbonate 2 ; distilled water 80. This operation should be conducted as rapidly and as aseptically as possible and there should be no delay in despatch. The material is used for injection of a guineapig or rats. *W. F. H.*

De la Barrera (J. M.). Estudios sobre peste selvática en Mendoza, [**Sylvatic Plague in Mendoza.**]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1940. Dec. Vol. 9. No. 5. pp. 565–586. With 7 figs. & 1 map.

The 1937 epidemic of pneumonic plague in Mendoza, a province of the Argentine [this *Bulletin*, 1940, Vol. 37, p. 423], induced the legislature to pass a measure for the study of (1) the mode of preservation of the organism of sylvatic plague in the interval between one epidemic and another, and (2) the rôle played in infection by the domestic rat. An extensive survey was begun of rodents and their ectoparasites. In the course of this work a new rodent was discovered in the nitre regions. This has been named *Tympenoctomys barrerai* and is somewhat larger than a *Graomys*.

The relations of rural plague with that of the rat were specially studied and the same conclusion formed as had been arrived at before, namely, that sylvatic rodents had little contact with the domestic rat. This accounts for the comparative absence of human plague in the presence of widespread epizootic. It has arisen at places far removed from one another and where no possibility of importation could have taken place. It must have persisted as enzootic. Sylvatic plague is not merely a rodent infection : it is also a flea infection. With the diminution of the flea index in summer and the diminution of rodents by death during an epizootic, propagation of the disease becomes increasingly difficult. The consequence of this is that plague remains latent by reason of the reduction of acute cases.

Although sylvatic plague has not been accompanied by much human plague, its existence is undoubtedly to be regarded as a danger. Under conditions of great increase of the sylvatic fauna, as may happen with an abnormally abundant harvest of maize, the access of plague to man will be rendered easier : the reason for this is that contacts, within human habitations, of the plague-carrying *Rattus* and *Xenopsylla cheopis* with sylvatic infection are greatly facilitated thereby.

W. F. H.

Eskey (C. R.) & Haas (V. H.). **Plague in the Western Part of the United States.**—*Public Health Bull. No. 254.* Washington. 1940. pp. v+83. With 61 figs. [Numerous refs.]

This important work, some of which has already been abstracted [this *Bulletin*, 1939, Vol. 36, pp. 310, 968], is divided into the three

parts: Introduction of plague and its spread, flea investigations, and demonstration of plague infection by inoculation of parasites. Each of these parts has its summary, which is full of detail. The photomicrographs of fleas found on rats and on the various animals subject to sylvatic plague are clear and useful. Some of the points dealt with are:—

Plague spread gradually among wild rodents and attracted little or no attention till 1934, by which time it had spread over a vast region extending from the Pacific coast to the Rocky Mountains. The rodents affected and forming reservoirs of plague are divisible into the ground squirrels, the wood rats and the prairie dogs. It seems probable that plague has not yet reached beyond the Rocky Mountains. Although this epizootic condition is widespread it does not seem to have given rise to, or been accompanied by, domestic rat infection and this accounts likewise for the comparative infrequency of human infection.

Some 50 species of fleas have been found to infest the wild rodents of the Western States and these may show a certain degree of specificity for their hosts, but it is not quite complete. It is a mistake to judge of the degree of flea infestation solely from the insects which can be collected from the body of the captured animal, for this would leave out of account those which are to be found in nests and runways. Nevertheless, plague infected fleas are unlikely to survive for any length of time in abandoned nests. The fleas only become infected when the blood of the host contains a sufficiency of plague organisms. Thus, experimentally "only 32 per cent. of exposed fleas were infected by the blood of guineapigs found to contain over 10 plague organisms in each microscopic field . . . while not a single flea was infected when bouillon culture failed to show the presence of *P. pestis* in the blood of sick animals." It was found that most plague infected fleas harboured virulent organisms throughout their lives, the life span, after a flea had transmitted plague for the first time, being on the average 3 days, with occasional survivals of 7 to 11 days. Before the infected flea however could transmit plague a period of incubation, called extrinsic incubation, has to take place and this varied in experiments from 5 to 130 days. The period may be shortened by increases of temperature and by other factors, and it is obvious that the shorter the extrinsic incubation the more rapidly the disease will be disseminated. The life of the flea does not seem to be affected by plague infection until blockage occurs, when the flea dies of starvation.

When collecting fleas from rodents with a view to inoculating laboratory animals, it is necessary to bear in mind that chloroform and ether are apt to destroy *P. pestis*. It is better, therefore, to use cyanide gas for this purpose. It is also better to make flea inoculation tests as soon as possible after collection of the parasites during warm weather to avoid attenuation of the bacillus. "At ordinary refrigeration temperatures *P. pestis* harboured by fleas may retain their virulence for 3 to 6 months or longer." Again, a method of transportation of fleas to be used for inoculation of guineapigs is in 2 per cent. salt solution. This inhibits the growth of putrefactive and other bacteria. A final word is said on the importance of inoculation of the fleas of wild rodents as a method of detecting the existence of plague among them, because this is a more reliable and sensitive test than the examination and inoculation of the tissues.

W. F. H.

BYINGTON (L. B.). **Two Epizootics of Plague Infection in Wild Rodents in the Western United States in 1938.**—*Public Health Rep.* 1940. Aug. 16. Vol. 55. No. 33. pp. 1496–1501. With 3 figs.

A close watch is now being kept on undue mortality among wild rodents in the Western United States and the two epizootics here recorded are instances of how the advance of plague infection may be brought to the notice of the authorities. Lincoln County, Wyoming, is sparsely inhabited and is a rough rocky inter-mountain plateau, having a population distribution of 2·5 persons per square mile, with concentrations at mining centres and along the railroad. Mortality here occurred among ground squirrels (*Citellus*) and wood-chucks (*Marmota*). Collections of rodents were made, represented by numbers from 1 to 150, and each collection, whether of one or more individuals, was kept separate. The pooled ectoparasites from each collection were used for guineapig inoculation and gave 37 plague infections for 115 collections, or 32 per cent.

The epizootic in Catron County, North Mexico, was even more interesting, for the population has a distribution of only 0·4 persons per square mile and the area consists of high rugged mountains or desert mesa. Moreover, this "epizootic took place more than 150 miles from any other known plague infected region." In this case unusual mortality was noticed in prairie dogs (*Cynomys*) and proved to be due to plague.

The conclusions drawn are that :—"Epizootic outbreaks of plague in rodents are occurring in the Western United States. These are part of a widespread enzootic of the disease in many species of rodents . . . . No human cases were known to have been associated with the infection in rodents." *W. F. H.*

GIBBONS (R. J.) & HUMPHREYS (F. A.). **Plague Surveys in Western Canada.**—*Canadian Public Health Jl.* 1941. Jan. Vol. 32. No. 1. pp. 24–28.

These plague surveys refer to rats, rat fleas and similar surveys for sylvatic plague rodents. Each rat as it was captured was sealed into a paper bag, which prevented escape of its ectoparasites. The fleas were collected from the animals into 0·9 per cent. salt solution. Autopsies of the rats were conducted and the fleas sorted into species for the determination of the "*cheopis* index." The fleas were still usable for inoculation tests.

Sylvatic plague investigations in the Western provinces of Alberta and British Columbia followed the lines of those conducted in Washington, Idaho and Montana, which are the bordering provinces of the United States. "Ground squirrels with their ectoparasites formed the bulk of specimens collected," in particular *Citellus columbianus columbianus* and *Citellus richardsonii richardsonii*.

One case of suspected human plague in a farmer is referred to. He was in the habit of feeding mink on ground squirrels and the mink, which had been healthy before, began to die.

At present it is not known how infection in the wild rodents was introduced into Alberta, but it is obvious that this infection is "matter of concern because of the potential hazards involved." Sylvatic plague has not yet been found in British Columbia. *W. F. H.*

ROBERTS (Austin). **Mammals concerned in the Bubonic Plague and Rabies Problems in South Africa.**—*South African Jl. Sci.* 1935. Vol. 32. pp. 414–460.

BHATNAGAR (S. S.). **Bacteriological Studies on** *Pasteurella pestis* **and** *Pasteurella pseudotuberculosis*. **Part I. The Morphology, the Growth and the Dissociation of** *Pasteurella pestis*.—*Indian Jl. Med. Res.* 1940. July. Vol. 28. No. 1. pp. 1–15. With 6 figs. on 1 plate. [29 refs.]

The problem of antigenic potency is one of the highest importance for active prophylactic immunization and is bound up with such questions as the use of rough and smooth bacterial types, dead and living organisms, virulent and avirulent types, temperatures of incubation and the cultivation of organisms in bouillon or on agar. Material has been collected by the author from as many sources as possible in order to test out some of these problems for the plague bacillus and he had at his disposal 92 strains. He does not consider that the plague bacillus possesses a capsule of the well defined type like the pneumococcus. It has a structure, a most important structure from the point of view of immunization, which manifests itself as a halo round the body of the organism and has been described as the " envelope " of the plague bacillus. Strains of the plague bacillus can be divided into virulent and avirulent, while the avirulent are sub-divided into protective and non-protective with reference to their usefulness in immunization. Two of these protective avirulent strains, which have been used in living form for the inoculation of human beings, are the well known " Tjiwidej " from Java and the " E.V." strain of Madagascar.

For the study of the envelope of the plague bacillus an Indian ink method was used, with the addition of staining for one hour by a mixture of equal parts methyl alcohol and one per cent. methylene blue. All " virulent strains " were found to possess envelope substance in fairly large quantity. Protective avirulent strains also showed envelope substance, but not in the same quantity as the virulent, while non-protective avirulent strains had no envelope. It was found however that non-protective avirulent strains if grown on horse serum agar acquired envelope substance and in the process developed " the typical viscidity of a normal plague culture." In contrast to this phenomenon of elevation to normality, the envelope strains, whether " fully virulent " or " protective avirulent," could be made, by serial subculture on rabbit blood agar every 48 hours and continuous incubation at 37°C., to lose all trace of envelope substance. Temperature of incubation had a most important influence both on the envelope and the size of the body of the bacterium ; " It was consistently observed that the largest quantity of the envelope substance was produced " at 37°C. and reduction of this temperature " was found to be accompanied simultaneously with a decrease in the amount of the envelope substance as well as in the size of the bacterial cell." The conclusion has been reached that " the most suitable medium for the optimal development of the plague bacillus both from the point of view of the envelope and the bacterial body " is 10 per cent. horse serum agar and that addition of a carbohydrate results in the production of a large amount of envelope substance although the total growth is not so luxuriant. *W. F. H.*

BHATNAGAR (S. S.). **Bacteriological Studies on** *Pasteurella pestis* **and** *Pasteurella pseudotuberculosis.* **Part II. The Serology of** *Pasteurella pestis* **and** *Pasteurella pseudotuberculosis.*—*Indian Jl. Med. Res.* 1940. July. Vol. 28. No. 1. pp. 17–42. [22 refs.]

The organisms *Pasteurella pestis* and *P. pseudotuberculosis rodentium* are closely allied and have given rise to difficulty, on occasion, in the diagnosis of plague in rats. One great difficulty in separating the two organisms has been that of applying serological tests: in particular the preparation of stable suspensions and high titre sera for agglutination tests has been a stumbling block. This handicap appears to have been overcome by the author without resort to diminution of salt content in the suspending fluid, and at the same time he makes a contribution to the knowledge of the antigenic constitution of the two organisms.

It has been shown by the author that certain strains of the plague bacillus possess envelope substance and certain strains, especially the "non-protective avirulent," do not. Now it has been found that envelope substance interferes completely with the somatic type of agglutination; nevertheless, "where this structure was absent, although somatic agglutination took place, the results could not be interpreted correctly because of the salt and serum sensitivity" of suspensions even in such low concentration of salt as 0·1 per cent. Moreover it was found that even "non-envelope" plague strains when subjected to agglutination tests, showed a modicum of envelope substance which could not be detected morphologically. An accident revealed that *P. pseudotuberculosis* possessed no envelope substance at all; it also possessed a common soma antigen with *P. pestis*. It was this finding that enabled the author to prepare suspensions for testing somatic agglutination by admixture of these two organisms; these suspensions, which were made with normal salt solution and represented supernatant fluid of a suspension from a serum-agar culture after deposition of coarse clumps, were stable and were made up of single organisms. They were suitable for agglutination tests of envelope and somatic antigen and were also usable to immunize animals to give high titre sera. Comparative tests revealed that strains of *P. pseudotuberculosis* "belonging to group I, types A and B, gave the highest readings in agglutination tests against antiplague sera."

Human cases of plague in the state of recovery showed both envelope and somatic agglutinins, although of low titre. In the serological reactions, which involve the use of the two organisms plague and pseudotuberculosis, that between the plague bacillus and its homologous serum has been designated as envelope antigen-antibody reaction and that of *P. pseudotuberculosis* as somatic antigen-antibody reaction. The differences found between the two organisms, which may prove highly useful in the identification of the plague bacillus, its antigenic analysis and in the diagnosis of plague, are summed up in the antigenic composition of *P. pseudotuberculosis*. This organism may be made to develop a flagellar antigen, but it has no envelope antigen, only somatic antigen. The author's study has shown that "*P. pseudotuberculosis* may be stated to be possessed of somatic 'O' antigens of the following order: (1) An antigen shared by all the strains of this organism as well as by *Pasteurella pestis*—the common group antigen. (2) An antigen present only in certain strains of this organism—the

group specific antigen. (3) An antigen which characterizes individual strains—the type specific antigen." In conclusion the observations are made that "to obtain reliable results in the serology of plague and of pseudotuberculosis the use of live organisms should be preferred . . . . If, however, the employment of killed suspensions is desired, chemically treated plague bacilli and heat-killed organisms of pseudotuberculosis should be employed." *W. F. H.*

BURTON (E.) & HENNESSEY (R. S. F.). **An Unusual Case of Plague with Meningitis.**—*East African Med. Jl.* 1940. Oct. Vol. 17. No. 7. pp. 266–270.

A child aged three with history of fever, headache and cough of sudden onset, six days previously, was admitted to hospital with a temperature of 103°F. and looking ill; the spleen was palpable. A small superficial abscess over the anterior tibial muscles was opened, but no organisms were found in the pus. Treatment was by M. and B. 693: in six days the temperature was normal and the child looked well. Four days later there was a sudden rise of temperature. No malarial parasites were found and sulphapyridine treatment was given for 5 days, when the temperature returned to normal. Once more pyrexia and headache reappeared and now the signs of cerebrospinal meningitis were definite. The lumbar puncture fluid was turbid and escaped under great pressure. Anti-meningococcal serum was given, but the child died. Examination of the cerebrospinal fluid microscopically, culturally and by guineapig test showed that the organism isolated was *Pasteurella pestis*. It is suggested that the original subcutaneous abscess was a plague abscess and "that this was a case of subacute or chronic plague terminating in a haematogenous meningeal infection." *W. F. H.*

BONEBAKKER (A.). Serumtherapie bij pest. [**Serum Therapy in Plague.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1940. Oct. 22. Vol. 80. No. 43. pp. 2502–2511.

Of 154 plague patients admitted to hospital 111 were treated with serum. The non-treated were, however, not alternate cases. A considerable number of plague cases had also been treated in earlier years with bacteriophage. In his final judgment the author makes frank admission of inability to come to definite conclusions on the value of the treatment and says: "1. A definite verdict on the success of the serum cannot, out of the experience gained, be given either statistically or clinically. Further, it was not possible to say whether serum was better than bacteriophage. 2. The impression was formed that the serum did benefit the patient and should therefore not be withheld. 3. It should be given early, daily, in fairly large doses and continued until the temperature falls and the general condition has improved. 4. No serious results occurred from serum treatment although serum sickness was frequent."

The method of administration is of some interest. To begin with, a dose of 10 cc. was given intravenously, simultaneously with 10 cc. in and around the bubo. On the following days the same dose was given, half intravenously and half intramuscularly, for as many as five days.

Later, however, the dose was doubled; sometimes all of it was administered intravenously, and on one occasion for 12 successive days with total of 380 cc. serum. *W. F. H.*

OTTEN (L.). Het levende pestvaccin en zijn resultaten (1935–1939). [**Results of Living Plague Vaccine.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1940. Dec. 10. Vol. 80. No. 50. pp. 2878–2950. With 3 charts. [16 refs.]

This article sets out the results of a long period of work on plague vaccines and is divided into three main sections—experimental investigations, plague vaccination, and preparation of the plague vaccine.

i. *Experimental.*—Early work on the dead plague vaccines sometimes gave satisfactory results and sometimes negative results, whether the vaccine was the Haffkine bouillon vaccine, the German agar vaccine or Flu's phage vaccine. This led up to the conclusion of the author that it was not the particular type of vaccine which was responsible for the variation but the particular species of animal used in the testing. The domestic rat is the least susceptible to plague infection and the guineapig the most susceptible. It appeared also that the grade of susceptibility and the degree of immunity which could be reached were highly correlated so that the domestic rat, mouse, house rat and guineapig form an ascending series as regards susceptibility and a descending series as regards possibility of immunization. The outcome of these researches convinced the author of the impossibility of attaining a satisfactory immunity with dead vaccine in the house rat and the guineapig and led him to diverge to the trial of living vaccine. An accidental isolation of a strain of plague from a dead rat accelerated the research and culminated in the well-known advocacy of the use of living plague vaccine for human prophylactic inoculation. This was the famous strain " Tjiwidej " which had been preserved in deep stab serum agar culture at 5°C. for 4 months and was then found to be avirulent. Even in doses of 5 cc. of a bouillon culture, or a whole agar culture, it proved harmless to house rats and guineapigs. Nor was this avirulent condition altered by passage through animals. What was still more important, however, was the next finding that the Tjiwidej strain was not merely avirulent, but was highly and effectively immunizing even in the very susceptible test animals, the house rat and the guineapig. This proved to be the case not only for artificial infection, but for infections contracted under more natural conditions, such as by blocked flea transmission; the vaccinated animals showed a high degree of survival to the flea infection, in marked contrast to the non-vaccinated controls. Other points connected with the use of living vaccine were submitted to experimental investigation:—rapidity with which immunization could be affected; duration of the immunity; the spontaneous loss of virulence by virulent strains; isolation of avirulent variants; the antigenic potency of avirulent strains; reversal of potency according to test animal (Tjiwidej and Soemedanj for the house rat and guineapig respectively); the relative efficacy of a killed virulent bouillon vaccine and a living avirulent bouillon vaccine; efficacy of avirulent bouillon or agar cultures grown at different temperatures; conversion of a virulent to an avirulent plague with the help of bacteriophage. The results of all this experimental work are shown in 20 tables.

ii. *Plague Vaccination.*—The satisfactory result obtained in very susceptible animals like the rat and the guineapig with the living avirulent strain " Tjiwidej " suggested the next step : the immunization of man with this strain. The method of choice was the statistical one of alternate case vaccination. A preliminary trial on volunteers showed that a dose of one-fifth of an agar culture produced no serious local or general symptoms. The result of the large scale trial worked out at : 37,435 persons vaccinated, with 1·01 per thousand mortality and 44,757 non-vaccinated, with 4·75 per thousand mortality—a reduction to about 20 per cent. Deaths were confirmed as due to plague by means of lung and spleen puncture and laboratory examination. A clear-cut graph for the regency Bandoeng gives the plague deaths during the years 1932 to 1940. The numbers show markedly rapid reduction to zero from 1935 onwards and, by the inclusion of calculated numbers for non-vaccination, the graph demonstrates what the amount of reduction in mortality is supposed to have been.

iii. *Preparation of Plague Vaccine.*—Freshly prepared living Tjiwidej vaccine, even in a dose of a whole agar culture, is practically without reaction in the rat. With keeping, even in the cool room, and much more rapidly at room temperature, the bacilli die off, endotoxin is set free and the toxicity rises. It is necessary, therefore, if reaction is to be avoided, that the vaccine should, once it is issued, be used as quickly as possible. The vaccine will preserve its activity in the cool room for at least a month. Extreme care has to be taken to ensure the sterility of the vaccine. In the earliest years one-tenth agar culture was the dose for an adult and one twenty-fifth for children, but this dose was altered to one of one-fiftieth for all ages in 1938.

What of the possibility of recovery of virulence ? Experience with strains which have undergone spontaneous loss of virulence has shown, in practice, that this change is not reversible. *W. F. H.*

MALARIA.

Précis of Abstracts in this Section.

In letters to the *Lancet*, Hutton, Napier and Manson-Bahr (p. 333) all refer to malaria in ships' companies after the ships have called at a West African port (Freetown is named by two of the writers). Infection is contracted even if the ship lies well away from the shore, and is presumably due to mosquitoes blown aboard or brought in small craft coming alongside. In some cases the disease is not, and cannot be, diagnosed on board and it is important to remember the possibility and to give quinine or atebrin to every suspected case, since a number of deaths have occurred. Prophylactic atebrin (or the British equivalent mepacrine hydrochloride) is advised for ships calling at these ports, and the dosage suggested is 0·3 gm. daily for 7 days.

McMurdo (p. 333) records a lower incidence of malaria in troops during manoeuvres in the Philippine Islands during 1940 than during 1938 and 1939, and ascribes this reduction to the protective measures taken. These included mosquito bars [? nets], prophylactic quinine and the use of Bamber oil as a repellent.

Young *et al.* (p. 334) show that the peak of parasite segmentation in four patients infected with *P. malariae* changed when the patients reversed their sleep from night to day, but was not affected by light when two of the patients slept in lighted and two in darkened rooms.

Stratman-Thomas (p. 334) writes of the effect of temperature on the development of *Plasmodium vivax* in *Anopheles quadrimaculatus*. Details are given, and in general it was found that the parasite was more susceptible to unfavourably high than to unfavourably low temperatures and that the mosquito could survive higher and lower temperatures than could the developmental forms of the parasite.

Thomson (p. 335) has made a careful detailed study of the behaviour of *Anopheles minimus* in Assam. Although shading is effective in eliminating breeding in running water, shade in itself is attractive to the ovipositing female and to the larva ; shading is only effective if it is dense enough to prevent the growth of vegetation along the water margins and thus to increase the rate of flow. The gravid female prefers to oviposit in still water, and the larva, contrary to common belief, is ill adapted to resist water flow. Control, therefore, can be achieved by freeing the stream edges of vegetation even in the light, though which is the better method will depend on local circumstances. Indiscriminate shading may even lead to increase in oviposition. The absence of *A. minimus* from shallow stagnant rice fields is related to the fact that this water repeatedly attains a temperature of 41°C., which kills the larvae in 5 minutes, though the larvae of *A. hyrcanus*, *A. barbirostris* and *A. vagus* resist even higher temperatures.

Zwemer *et al.* (p. 336) show that in malaria there is an increase of potassium in the blood plasma which is marked just before the rises in temperature. The possible origins of this potassium are discussed and it is thought that potassium may be the toxic substance released from the red cells at the time of rupture.

Stratman-Thomas and Dulaney (p. 336) failed to obtain positive skin reactions or precipitin tests in cases of malaria, even though several antigens were used. They found that the complement fixation reaction, however, yielded highly specific results with antigens from human or monkey blood containing parasites, and describe the preparation of this antigen.

Sanford *et al.* (p. 337) report on cases of malarial coma admitted to a hospital in Tennessee during five years.

Wilkinson (p. 337) records three cases of mental derangement which followed the administration of atebrin. All made rapid recoveries.

Shortt and Menon (p. 338) failed to produce immunity in monkeys inoculated with killed parasite substance prepared from *P. knowlesi* by the method of Christophers and Fulton. The method is described. They (p. 338) have infected monkeys and fowls by allowing blood heavily infected with relevant parasites to drop into their mouths.

Mulligan and Russell (p. 338) show that sporozoites of *P. gallinaceum* are clumped by normal animal sera, but more readily by sera of animals with malaria, and most of all by sera of fowls chronically infected by the homologous parasite. *C. W.*

HUTTON (E. L.); NAPIER (L. Everard); MANSON-BAHR (Philip). **Malaria on Board Ship.** [Correspondence.]—*Lancet.* 1940. Nov. 9 & 30. pp. 603; 696.

i. The first correspondent refers to a report that a ship's company suffered a high mortality rate from malaria after calling at a West African port, in spite of the prophylactic issue of quinine. He recommends the substitution of atebrin for quinine; the former, unlike quinine, is a true causal prophylactic. A drug identical with atebrin is now being manufactured in England.

ii. The second letter reports the occurrence of four cases of malaria on board a ship. Infection in some, if not in all, of these cases was acquired at Freetown although the ship was anchored well over a mile from the shore. Infected mosquitoes may have been blown from the shore, the most likely speculation, or they may have been brought by an oil-lighter, motor launches, or country boats, all of which came alongside.

iii. Reference is made to the large number of seamen and passengers arriving in London with severe infections of subtertian malaria, the infection of which had been acquired in the harbour of Freetown. Given a favouring wind and other conditions malaria infection may be contracted in any location in Freetown harbour, however far from the shore. In some cases the stay in Freetown harbour had been less than 12 hours. In some cases malaria had not been diagnosed on board ship and deaths occurred. Subtertian malaria should be suspected in every case of sudden illness arising ten days or more after leaving the west coast of Africa. Quinine or atebrin should be given to every suspicious case, in the absence of microscopical diagnosis which usually is impossible on board ship. The author recommends a prophylactic course of atebrin, 0·3 gm. a day for 7 days, during the voyage home. A product identical with atebrin, mepacrine hydrochloride, is now being manufactured in England. *Norman White.*

McMURDO (H. B.). **Malaria, 1940 Maneuvers, Luzon, Philippine Islands.**—*Milit. Surgeon.* 1940. Sept. Vol. 87. No. 3. pp. 252–255. [Summary taken from *Public Health Engineering Abstr.* Washington. 1940. Dec. Vol. 20. No. 12. p. 12. Signed H. A. JOHNSON.]

"The Malaria records for the 1940 army maneuvers were very low in comparison to the 1938 and 1939 rates. This doubtless resulted from the general knowledge relating to the breeding habits of A. minimus promulgated to all branches of the army. In view of this knowledge camp sites were more appropriately selected with reference to A. minimus habits. Mosquito bars were systematically employed, prophylactic quinine in 5 grain doses was routinely used, and Bamber oil was used as a repellant. In view of the observations made it was recommended for future maneuvers that the Medical Department play an active role in the selection of camp sites, that mosquito bars be employed and inspected for tears, etc., daily; that mosquito bars be provided with an 18 in. border of unbleached muslin; that quinine be routinely employed in daily doses of 5 grains as a prophylactic measure, and that Bamber oil be used externally as a repellant. It is of interest that the withdrawal of all quinine is recommended immediately upon return from maneuvers."

YOUNG (Martin D.), COATNEY (G. Robert) & STUBBS (Trawick H.). **Studies on Induced Quartan Malaria in Negro Paretics. II. The Effect of modifying the External Conditions.**—*Amer. Jl. Hyg.* 1940. Nov. Vol. 32. No. 3. Sect. C. pp. 63–70. With 4 figs.

This is a continuation of a study on quartan malaria the first part of which dealt with the periodic phenomena of the asexual cycle [see this *Bulletin*, 1940, Vol. 37, p. 783]. In the four patients studied segmentation of the parasites reached its height at 9·0 a.m. with remarkable constancy. After the infection and the periodic phenomena had become established the external conditions of these patients were reversed. Night was turned into day, and *vice versa*. The patients slept all day, two in a dark and two in a well-lighted room; they were up all night in a well-lighted room and had meals at 7.0 p.m., midnight and at 7.0 a.m. In the patients who were kept continuously in the light the peak time of segmentation changed from 9·0 a.m. to 9·0 p.m. When one of these patients returned to normal conditions the peak time again appeared at 9·0 a.m. In one of the other two patients a similar change was observed; in the other the cycle was shortened until the peak occurred 22 hours earlier than normally expected. Thus the reproductive activity of *P. malariae* in man is markedly affected by the conditions of the host; light, whether continuous or intermittent, has no effect. *N. W.*

STRATMAN-THOMAS (Warren K.). **The Influence of Temperature on** *Plasmodium vivax.*—*Amer. Jl. Trop. Med.* 1940. Sept. Vol. 20. No. 5. pp. 703–715.

Control and experimental lots of insectary-reared *A. quadrimaculatus* were fed upon paretics undergoing malaria therapy with a strain of *P. vivax*. The blood of the patients selected contained gametocytes; exflagellation was always demonstrated before anophelines were applied. The fed mosquitoes were transported from the hospital to the laboratory, where they were placed in incubators at various temperatures. The time occupied in transit was from one to one and a half hours: during this time the mosquitoes were kept at about 28°C. For the various temperatures there were two large incubator rooms kept at 37·5°C. and 28°C.; a small electric incubator adjusted to temperatures of 26°, 30° and 32°C.; an air-conditioned insectary kept at 22°C., later changed to 24°C.; and a frigidaire with thermostatic control for temperatures from 15° to 17°C. and below. The cycle of sporogony was completed within the temperature range of 15–17° to 30°C. The shortest time for the completion of the cycle was 8 days, at 28° and at 30°C, and the longest time 38 days, at 15–17°C. At all stages of the cycle *P. vivax* was more susceptible to unfavourably high temperatures than to unfavourably low temperatures. Shortly after feeding, an infected *A. quadrimaculatus* was completely sterilized of its infection in 2 to 3 hours at 37·5°C.: at 1° to 10°C. two and a half days' exposure was necessary to secure this result. During the growth of oöcysts, 7 to 13 days after feeding, exposure of the mosquito to 37·5°C. for 18 to 24 hours aborted the development of the parasite: at 1° to 10°C. 24 days' exposure was necessary to interrupt oöcyst development. When sporozoites were present in the salivary glands 24 hours' exposure to 37·5°C. inhibited the infectivity of the sporozoites

for human inoculation. Adult *A. quadrimaculatus* can survive higher and lower temperatures than can the developmental forms of *P. vivax* which it may harbour. *N. W.*

THOMSON (R. C. Muirhead). **Studies on the Behaviour of *Anopheles minimus*. Part I. The Selection of the Breeding Place and the Influence of Light and Shade.**—*Jl. Malaria Inst. of India.* 1940. Sept. Vol. 3. Nos. 2 & 3. pp. 265–294. With 3 figs., 4 graphs & 9 plates. [23 refs.] **Part II. The Influence of Water Movement on the Selection of the Breeding Place.**—*Ibid.* pp. 295–322. With 9 figs., 2 graphs & 4 plates. **Part III. The Influence of Water Temperature on the Choice and Suitability of the Breeding Place.**—*Ibid.* pp. 323–348. With 3 graphs, 1 fig. & 3 plates. [11 refs.]

The author of these papers is making a systematic study, in the field and in the laboratory, of the factors in the environment which limit the breeding of *Anopheles minimus* in Assam to certain well defined types of water. He deals here with the factors of light and shade, water movement and temperature. He has already pressed the analysis of the behaviour of this mosquito further than has previously been achieved with any other Anopheline species.

It is characteristic of *A. minimus* that it nearly always breeds in running water with grassy edges and that it may be eliminated from these breeding places by shading them heavily with vegetation. But the author shows that shade in itself is highly attractive to the ovipositing female. She lays her eggs normally at night, mostly in the first third of the night, but even at this low level of illumination the effects of shade are very important : she will not lay eggs in an unshaded position. Normally the necessary degree of shade is provided by grass, etc., along the water margins ; but indiscriminate shading of the breeding places may well lead to an increase in oviposition.

Shading is effective as a method of control only if it is dense enough to produce certain secondary effects. The most important of these is the elimination of vegetation from the water margins with a consequent increase in the rate of flow. This acts in two ways. (i) The gravid female prefers to oviposit in still water and will avoid water flowing even at a rate of 1 foot in 20 secs. Practically still water is to be found in the streams only in the grassy edges or in side pockets. (The female will oviposit in shaded side pockets of still water completely devoid of vegetation). Oviposition in densely shaded streams is thus prevented by the increased water movement that results from the exclusion of all grass and other plants. (ii) Contrary to the popular belief, the larva of *A. minimus* is ill adapted to resist being carried away by flowing water. It lives normally in the still water at the edge of the stream ; it cannot resist a rate of flow greater than 0·29 foot per sec. It is normally maintained in this still water, not by an avoidance of moving water, but by a very powerful attraction to shade. This reaction is intensified by water movement ; it is so strong that under experimental conditions larvae can be induced to leave an unshaded zone of still water in favour of a shaded zone with a current great enough to sweep them downstream. (The author analyses this response in terms of recognized mechanisms of orientation.)

Control by dense shading is therefore due to prevention of oviposition by the gravid female and the sweeping away of larvae by the increased current. The same results may be achieved by exposing the streams

to light and freeing the edges completely of vegetation. (By this means the breeding of *A. minimus* is excluded naturally from many of the perennial rivers of the foot-hill region.) Which is the better method to employ will depend on local circumstances.

In Part III the author studies the temperature of different types of anopheline breeding place in the field, and the upper temperature limits for the early stages of a number of anopheline species in the laboratory. The absence of *A. minimus* from shallow stagnant rice fields is related to the fact that during the daytime these collections of water repeatedly exceed 41·0°C., the temperature which will kill full-grown larvae of *A. minimus* in 5 minutes, whereas *A. hyrcanus* and *A. barbirostris*, which breed normally in such places, have a thermal death point of 43·5°C., while *A. vagus*, which abounds in shallow pools of all kinds, can survive up to 45·0°C. Such high temperatures may still be attained in the fields when the rice shoots, 9 inches apart, are 2 feet high ; whereas the maximum temperature in the running water breeding places of *A. minimus* seldom exceeds 35°C. During the night these differences in water temperature no longer hold ; and yet the egg-laying female of *A. minimus* avoids the stagnant rice fields. By what means she is able to do so is a problem which remains to be solved. *V. B. Wigglesworth.*

ZWEMER (R. L.), SIMS (E. A. H.) & COGGESHALL (L. T.). **The Plasma Potassium Level during Malaria Infection in Monkeys and Man.**—*Amer. Jl. Trop. Med.* 1940. Sept. Vol. 20. No. 5. pp. 687–701. With 1 chart. [21 refs.]

During malaria infections the rupture of merozoites from red cells releases a toxic substance. Since red cells contain twenty or more times as much potassium as plasma it is possible that potassium is this toxic substance. To test this hypothesis studies were made on thirteen patients undergoing malaria therapy with *P. vivax*. Additional studies were made on rhesus monkeys inoculated with *P. knowlesi*. It was shown that in malaria of man and monkey there is an increase of potassium in the plasma and serum which may come from red cells at the time of sporulation of the parasite, or may result from the reaction of foreign protein or toxin on body cells in general. This marked increase in potassium is accompanied by chills and precedes the rise in temperature. The base line potassium values tend to increase with progress of the malaria infection. It is pointed out that marked involvement of the adrenal cortex in some fatal malaria cases is compatible with a disturbance in potassium metabolism.

N. W.

STRATMAN-THOMAS (W. K.) & DULANEY (Anna Dean). **Immunologic Studies in Malaria with Special Reference to the Diagnosis of Malaria.**—*Amer. Jl. Trop. Med.* 1940. Sept. Vol. 20. No. 5. pp. 717–725. With 1 fig.

In 268 skin tests in cases of malaria the authors failed to obtain a single reaction which could be regarded as specific for malaria, using as antigens a papain digest of human plasmodia [SINTON & MULLIGAN, this *Bulletin*, 1933, Vol. 30, p. 492] ; watery extracts of blood clots from heavily parasitized individuals [HERMANN & LIFSCHITZ, this *Bulletin*, 1930, Vol. 27, p. 650] ; washed red cells from heavily

parasitized blood laked with distilled water ; saline extracts of parasites centrifuged after laking of red cells ; NaOH digests of parasites ; and sera of infected patients.

With various antigens prepared from infected human and from infected monkey blood 388 precipitin tests were carried out, of which 287 were on the sera of malaria patients. No specific precipitin reaction could be demonstrated.

For complement fixation infected and normal monkey antigen and infected and normal human antigen were used. The monkey antigens and the normal human antigen were prepared after the method of COGGESHALL & EATON [this *Bulletin*, 1939, Vol. 36, p. 404]. The infected human antigen was prepared from parasites centrifuged from laked heavily parasitized blood cells. The parasite mass was dried *in vacuo* and ground. A measured amount was rehydrated, frozen, thawed, centrifuged, and the supernatant fluid used as antigen. Sixty-two patients with malaria and 35 normal persons were tested. Infected monkey and infected human antigens gave identical results. Patients with malaria parasites in their blood at the time the sera were taken gave a significantly higher number of positive reactions than those with no parasites. Patients having fever before sera were taken gave significantly more positive reactions than those who had not had fever. In short, the complement fixation test yields highly specific results in malaria with antigens prepared from either human or monkey parasitized blood. *N. W.*

SANFORD (Conley H.), CRAWFORD (P. T.) & WARR (Otis S.). **Malarial Coma.**—*Ann. Intern. Med.* 1940. July. Vol. 14. (O.S. Vol. 19). No. 1. pp. 72–77. With 1 fig.

During five years 1,021 patients were admitted to the John Gaston Hospital, Memphis, Tennessee, in a comatose condition. Malaria was the cause of coma in 48 of these cases, 4·7 per cent. In one year of the five, malarial coma cases were as numerous as 8·5 per cent. of the total malaria admissions ; in another as low as 0·9 per cent. Most of the patients with malarial coma were admitted in August and October ; none was admitted in the months of February to June, inclusive. The unusual feature of this series of cases of malarial coma is that three of them were ascribed to *P. vivax* infections. Brief notes of these three cases are given. *P. vivax* was found in the blood smears. [It might be pointed out that failure to find *P. falciparum* in blood smears does not preclude the possibility of a *P. falciparum* infection.] The case mortality rate of the series was 40 per cent. *N. W.*

WILKINSON (P. B.). **Mental Disturbance after the Exhibition of Atebrin.**—*Caduceus.* Hong Kong. 1939. Nov. Vol. 18. No. 4. pp. 267–271.

Three cases are described in which mental derangement followed the use of atebrin in the treatment of malaria. One patient was Dutch and the other two Chinese ; the former had a history of previous mental instability. All three made rapid recoveries. The doses of atebrin used were not excessive and none had pigmentation of the skin or gastro-intestinal disturbance. *N. W.*

SHORTT (H. E.) & MENON (K. P.). **Attempt to produce Active Immunity to Malaria in Monkeys by Vaccination with Parasitic Substance.**—*Jl. Malaria Inst. of India.* 1940. June. Vol. 3. No. 1. pp. 191–193.

Attempts were made to immunize two monkeys (*Macaca radiata*) by giving them six weekly injections of parasite substance prepared from *M. rhesus* infected with *Plasmodium knowlesi*. The substance was obtained by exposing infected blood to the action of saponin according to the method of CHRISTOPHERS and FULTON [see this *Bulletin*, 1940, Vol. 37, p. 190], by which the red blood corpuscles are destroyed and the parasites liberated. After washing, the parasites, which are still infective, are killed by grinding in a mortar with carborundum powder. The ground material was suspended in saline solution and the carborundum allowed to settle. The saline suspension of parasite substance was decanted and was used as the vaccine. Neither monkey developed any effective immunity against intraperitoneal inoculation of the homologous parasite.

C. M. Wenyon.

SHORTT (H. E.) & MENON (K. P.). **Experimental Production of Monkey and Avian Malaria by an Unusual Route of Infection.**—*Jl. Malaria Inst. of India.* 1940. June. Vol. 3. No. 1. pp. 195–198.

The paper describes experiments in which *M. rhesus* were infected with *Plasmodium knowlesi* and fowls with *P. gallinaceum* by allowing heavily infected blood to drop into their mouths, care being taken not to injure the mouth during the administration of the blood and that no obvious lesion existed in the mouth. *C. M. W.*

MULLIGAN (H. W.) & RUSSELL (Paul F.). **Agglutination of Sporozoites of *P. gallinaceum*. Preliminary Note.**—*Jl. Malaria Inst. of India.* 1940. June. Vol. 3. No. 1. p. 199.

This is a preliminary note to announce the observation that sporozoites of *Plasmodium gallinaceum* are clumped by normal sera of various animals and man, more readily by sera of animals which have suffered from malaria and most readily by the serum of fowls chronically infected with the homologous parasite. In the last case definite agglutination was observed with a 1/8000 dilution of the serum.

C. M. W.

BLACKWATER FEVER.

PRÉCIS OF ABSTRACTS IN THIS SECTION.

FAIRLEY (p. 339) sums up his work on the katabolism of human and monkey haemoglobin when incubated *in vitro* with human or monkey serum. There are three stages: (1) The production of neutral or alkaline methaemoglobin, (2) the splitting of methaemoglobin into globin and haematin (ferric), and (3) the coupling of haematin (ferric) to serum albumin to form methaemalbumin.

DE NAVASQUEZ (p. 340) believes that the mechanical theory of the blockage of renal tubules by methaemoglobin in acid urine as the cause of renal insufficiency in blackwater fever and in incompatible blood transfusion is wrong. In experiments on rabbits, into which haemoglobin was injected daily, he found that in the three hours following each injection, rabbits secreting acid urine passed methaemoglobin, while those secreting alkaline urine passed oxy-haemoglobin. Those with acid urine passed more iron than those with alkaline, and the author takes this as an indication that in the acid urine group the tubules were not blocked with haemoglobin products, so long as there was an adequate flow of urine. He suggests an extreme fall in blood pressure as a cause of anuria in incompatible blood transfusion.

HADEN (p. 342) discusses haemolytic anaemia, giving an abnormal shape of the red blood cells as a possible cause of the excessive blood destruction. When a cell is injured it tends to assume a spherical shape, and in haemolytic anaemia there may be congenital spherocytosis ; a spherocyte is more easily haemolysed than a biconcave disc, since a sphere has smaller surface area than a disc, in relation to its volume, and cannot therefore undergo as much stretching as a disc.

SZIGETI (p. 343) describes the estimation of oxyhaemoglobin and methaemoglobin by means of a photo-electric colorimeter.

DOWDS (p. 343) reports blackwater fever in a S. African native who had been undergoing treatment with quinine followed by plasmoquine ; after 3 days' treatment with the latter the methaemoglobinuria developed. So (p. 344) reports three cases of blackwater fever in which quinine had not been given. Two of the patients had received plasmoquine.

FOY and KONDI (p. 344) describe the appearances seen at post mortem of a premature infant born of a woman suffering from blackwater fever. There was no trace of methaemoglobin and there were no malaria parasites in the blood of the infant though the placental blood was loaded with schizonts of *P. falciparum*. It would appear, therefore, that methaemoglobin does not pass the placenta. The authors discuss possible explanations. *C. W.*

FAIRLEY (N. Hamilton). **The Spontaneous Disintegration of Certain Blood Pigments, with Special Reference to Methaemalbumin Formation.**—*Brit. Jl. Experim. Path.* 1940. Aug. Vol. 21. No. 4. pp. 231–242. [11 refs.]

In the introduction to this paper the author briefly reviews the conclusions he has reached regarding the disintegration of certain blood pigments, with special reference to methaemalbumin formation. Most of this work has already been published elsewhere and noticed in this *Bulletin*.

The present paper describes the technique used and the actual experiments on which these and subsequent conclusions have been based. The paper is of a somewhat technical nature, and must be consulted in the original by those interested.

The following are the summary and conclusions :—

" (1) When a haemoglobin-plasma system is incubated (37° or 40°C.) neutral methaemoglobin is produced in the early stages, which is liable to be converted into alkaline methaemoglobin owing to a shift in *p*H of plasma to the alkaline side of 8·0.

" (2) When an aqueous solution of haemoglobin is incubated alone this alkaline shift is absent and only neutral methaemoglobin is demonstrable.

" (3) Where oxalated whole blood is incubated (37° or 40°C.) no alkaline shift in the *p*H is observed in the sedimented corpuscles which ultimately contain neutral methaemoglobin ; in the plasma, owing to the alkaline shift, alkaline methaemoglobin is formed.

" (4) If the plasma in the system be derived from man and monkeys a pigment—methaemalbumin—with an α band at 623$\mu\mu$ to 624$\mu\mu$ appears within 48 hours and increases progressively—apparently at the expense of methaemoglobin.

" (5) After a period of incubation at 37°C. for 10 days methaemalbumin is present in considerable concentration ; it can be isolated in the albumin fraction entirely free from haemoglobin or methaemoglobin ; on drying *in vacuo* over sulphuric acid a brown solid residue is formed containing methaemalbumin which is water-soluble and present in a stable and relatively pure form.

" (6) The conclusion reached is that *in vitro* there are three stages demonstrable in the katabolism of haemoglobin incubated in the presence of human or simian plasma : (1) The production of neutral and alkaline methaemoglobin, (2) the splitting of methaemoglobin into globin and haematin (ferric), and (3) the coupling of haematin (ferric) to serum albumin to form methaemalbumin.

" (7) With rabbit plasma and that of many other mammals the pigment produced in the later stages of incubation resembles haematin (ferric) spectroscopically, but there is some evidence that even here a haematin-albumin compound is formed." *W. Yorke.*

DE NAVASQUEZ (S.). **The Excretion of Haemoglobin, with Special Reference to the " Transfusion " Kidney.**—*Jl. Path. & Bact.* 1940. Nov. Vol. 51. No. 3. pp. 413–425. With 1 chart. [11 refs.]

In 1925 BAKER and DODDS showed that the reaction of the urine, which could be controlled by diet, was a factor in determining the results obtained by transfusing rabbits with homologous haemoglobin. Thus, if the urine were alkaline, as it normally is in a rabbit receiving abundant green food, the haemoglobin was excreted without difficulty and unchanged. If, however, it were acid, brown precipitates appeared in the medullary tubules of the kidney, brown casts of haemoglobin derivatives, which were thought to be methaemoglobin and acid haematin, occurred in the urine, the urinary secretion was reduced and the amount of urea in the blood increased. It was believed that the basis of this anuria and azotaemia was a mechanical blockage of the renal tubules by methaemoglobin. Similar findings had been noted in man in blackwater fever and as a result of incompatible blood transfusions ; so that these experimental results have been widely accepted as the explanation of the fatalities which commonly result from the latter. More extended and more recent experiences of this condition have raised doubts if such an explanation suffices.

In the paper under review de Navasquez records three cases of anuria and death following blood transfusions, in spite of the administration of alkalies ; he also describes experiments on rabbits, analogous to those of Baker and Dodds, which, however, have given him quite different results and from which he concludes that the theory of mechanical blockage of the tubules as causal of the renal

insufficiency is wrong. In these experiments de Navasquez used a solution of purified rabbit haemoglobin of 50 per cent. strength (Haldane) which was injected in doses of 10–15 cc. The injections usually were made daily. The urine was obtained by catheter and its iron content estimated. The blood urea was followed and when an animal died or was killed the iron content of one kidney was determined. Most of the rabbits received from two to five injections, the maximum number being thirteen. The animals were divided into two groups, in one of which the urine was kept acid and in the other alkaline. The majority of the animals survived the injections and were killed for examination.

The duration of the experiments was from one day up to several weeks, the longest (on acid producing diet) being nine weeks, the animal receiving thirteen injections of haemoglobin.

[From the estimations of the iron content of the injections the dosage in terms of blood would appear to have ranged from 2·5 cc. to 16·8 cc. and in just over a half of the experiments to have been the equivalent of rather less than 5·0 cc. of blood per animal.]

The results, which are summarized in the paper, show that in the three hours which succeeded each injection the thirteen rabbits which were secreting an acid urine all passed dark-coloured chocolate-brown urine, which gave the absorption bands of methaemoglobin. A number lost weight and showed a raised blood urea, but the urinary urea was also raised ; the phenol red excretion test was normal and it is stated that there was no oliguria. In rabbits maintaining an alkaline urine the haemoglobin was excreted as oxy-haemoglobin. The phenol red excretion was normal and some animals showed an increase in blood urea.

The excretion of iron differed notably in the two series. In the " acid " group a mean of 30 per cent. of the injected iron was excreted in the first three hours of the experiment, while in the " alkaline " group only about 15 per cent. was excreted in the same time. This difference was reflected in the kidneys, those of the " acid " group becoming iron-free in some three to four days, while those of the " alkaline " group retained iron for considerably longer periods. Histologically Perles's reaction for iron was negative in the " acid " kidneys, but there was a " slight bluish haze " in the cytoplasm of the cells of the convoluted tubules in the " alkaline " kidneys. A precipitate of brownish material was seen in the convoluted and collecting tubules of animals in the " acid " series which were killed within a few hours of the haemoglobin being injected, and clear reddish matter in these situations in the " alkaline " kidneys ; these findings were no longer present 24 hours after the injections. No other renal changes of importance were noted. The spleen showed free iron, as did the Kupffer cells of the liver in some cases. The liver showed focal necroses in four animals which had received repeated injections of haemoglobin. The rapid clearance of iron from the kidneys of the acid group is taken as evidence against the theory of Baker and Dodds, since, if these tubules were blocked with haemoglobin products, iron retention would be expected. De Navasquez supposes that the dissolved haemoglobin of an alkaline urine is more freely absorbed in the renal tubules [and retained in them ?] than the precipitated haemoglobin of an acid urine. The latter, however, does not remain in the kidney but is rapidly removed if there is an adequate urinary flow. To explain the oliguria and anuria of incompatible blood transfusion he

postulates a failure of glomerular secretion but finds no histological evidence of this. He suggests it may be due to an extreme fall in blood pressure.

[Although at first sight they are contradictory, it seems possible to reconcile these findings with those of Baker and Dodds. In many cases in which workers at the same problems have got different results in similar experiments, the explanation has ultimately been found to lie in a difference in technique. The obvious point upon which information is required, before the two series of experiments can be compared, is the quantity of haemoglobin injected by the different workers. De Navasquez's doses are on the whole moderate, when compared, for example, with those given by DeGowin, and others (*Arch. Intern. Med.*, 1937, Vol. 59, p. 432 ; 1938, Vol. 61, p. 609) in comparable experiments on dogs. The amounts injected by Baker and Dodds are not stated in a form which allows comparison, but it would seem that their doses must certainly have been vastly greater than those given by de Navasquez. If this be the case, most of the differences in results may be explained. In comparing such experiments with the effects of incompatible blood transfusion in man, the reader is struck with the small amount of incompatible blood which will produce a fatal result in man. It does appear that the earlier workers may have been too ready to accept the attractive doctrine of simple blockage of the renal tubules, produced by acid and salt precipitation of haemoglobin products, as a sufficient explanation of the much graver conditions which occur in man in certain cases of transfusion. Recent observations upon anuria in cases of shock treated by transfusions of plasma or serum point to the presence of other factors than simple intravascular haemolysis and kidney tubule blockage. The elucidation of these is one of the problems of the moment.] *J. Henry Dible.*

Haden (Russell L.). **Hemolytic Anemia.**—*Jl. Lab. & Clin. Med.* 1940. Oct. Vol. 26. No. 1. pp. 65–81. With 7 figs. [18 refs.]

It is difficult to do justice to this interesting and instructive paper in a short abstract, and the reviewer feels that he cannot do better than reproduce the author's own summary, which is as follows :—

" A hemolytic anemia is due to an excessive destruction of red blood cells beyond the compensatory capacity of the bone marrow to deliver new cells.

" The normal red blood cell has a delicate structure which may be injured in many ways. The biconcave shape results in a state of strain in the stroma.

" As erythrocytes are destroyed, iron is set free, and bilirubin is formed as the end product of hemoglobin destruction.

" The clinical picture of a hemolytic anemia is an anemia with jaundice and an enlarged spleen.

" The laboratory study in a hemolytic anemia shows a high reticulocyte count from excessive marrow activity, a high icterus index, and a hyperplastic bone marrow.

" The excessive destruction of red blood cells in a hemolytic anemia may result from (1) damage to the red blood cells, (2) an abnormal shape of the red blood cells, (3) a congenital defect in quality of stroma, or (4) an overactivity of the spleen.

" The mechanism of hemolysis varies with the hemolytic agent.

"When a cell is injured, it tends to assume a spherical shape since the strain incident to the biconcave shape is released.

"The most characteristic and clinically important hemolytic anemia is congenital spherocytosis or congenital hemolytic icterus. The inherited defect here is the abnormal shape of the red blood cell.

"A spherocyte is more easily hemolyzed than is a biconcave disk.

"There is a direct relationship between hypotonic fragility of the red blood cell in spherocytosis and its shape. A sphere has a smaller surface area in relation to volume, so it can undergo less stretching before hemolysis occurs than a biconcave disk.

"The anemia disappears after splenectomy in congenital hemolytic icterus. The spherocytosis persists, but it is less marked.

"Spherocytosis may be acquired since an injury to cells by any agent may cause it. Acquired spherocytosis is characterized by increased fragility of cells.

"In many hemolytic anemias there is no abnormality of shape so the hemolysis must depend upon other factors, such as an abnormal reaction, changes in the cell membrane, stroma, or constituents of the plasma, or abnormal reticulo-endothelial activity.

"In sickle-cell anemia and in the erythroblastic anemia of Cooley, there seems to be a congenital defect in the stroma which allows the cells to be easily hemolyzed abnormally.

"If hemoglobinuria is present in a hemolytic anemia, the cells are being destroyed in the circulating blood and not in the spleen.

"With hemoglobinemia and hemoglobinuria, splenectomy is contra-indicated."

W. Y.

[This paper is not concerned directly with blackwater fever, but it is of sufficient interest to warrant its inclusion in this section.—*Ed.*]

SZIGETI (B.). **Estimation of Oxyhaemoglobin and of Methaemoglobin by a Photoelectric Method.**—*Biochem. Jl.* 1940. Nov. Vol. 34. Nos. 10 & 11. pp. 1460–1463. With 1 fig.

The author states that the oxyhaemoglobin content of blood can be rapidly and accurately measured by means of a photoelectric colorimeter. In the absence of oxyhaemoglobin or of other pigments, methaemoglobin can be determined in the same way; and in whole blood the presence of met- or of sulph-haemoglobin or of other pigments can be detected. It was found that the use of 0·4 per cent. ammonia as a diluent for blood for spectrophotometric measurements is not safe, and that better results can be obtained with a concentration of 0·04 per cent. ammonia.

The photoelectric colorimeter used was a Hilger Absorptiometer (Hilger, 1936) and the method adopted is described in detail. The subject is rather technical and the original should be consulted by those interested. *W. Y.*

DOWDS (J. H.). **Blackwater Fever in an African Native.**—*South African Med. Jl.* 1940. Sept. 28. Vol. 14. No. 18. p. 365.

The author states that this is the first case of blackwater fever encountered in the course of ten years among a native population averaging about 15,000, in a malarious country in which the disease is common among the small European population.

The patient was 25 years of age and had lived all his life in the district. After he had been in hospital for a week undergoing treatment for a recently acquired simple conjunctivitis, a routine blood

examination revealed a few malignant tertian rings and crescents. The temperature had been normal throughout his stay in hospital. Quinine, gr. 30, was given for seven days, followed by plasmoquine 0·02 gm. thrice daily. After three days' treatment with the latter he passed a large quantity of dark brown urine containing methaemoglobin. The temperature rose to 103°, the pulse to 130 and the patient vomited frequently during the next 24 hours. The following day the vomiting ceased, and a mild degree of jaundice was noted. The methaemoglobinuria continued for three days, at the end of which the haemoglobin was reduced to 32 per cent. The convalescence was uneventful. [Probably the plasmoquine had something to do with the development of methaemoglobinuria in this case.] *W. Y.*

So (Teiju). **Cases of Blackwater Fever without Administration of Quinine.**—*Taiwan Igakkai Zassi* (*Jl. Med. Assoc. Formosa*). 1940. Nov. Vol. 39. No. 11. [In Japanese pp. 1850–1861. [32 refs.] English summary pp. 1861–1862.]

Details are given of three patients who were stated to have developed blackwater fever without previous administration of quinine.

The first patient suffered from malignant tertian malaria, and was treated with atebrin and subsequently with plasmoquine, 0·03 gm. daily. After three days of plasmoquine he suddenly developed blackwater.

The second patient, a man of 58, was admitted to hospital with enteric fever. He gave a history of having previously suffered from malaria for several years. When recovering from typhoid, he suddenly had a rigor with high fever, and next day was found to be suffering from blackwater fever. Examination of the blood showed malarial parasites, as was expected [*sic*]. This patient had apparently not received any of the usual malarial remedies, *e.g.*, quinine, atebrin or plasmoquine, before the blackwater developed.

The third patient was apparently suffering from her first attack of malaria when admitted to hospital. She was treated with atebrin 0·3 gm. plus plasmoquine 0·03 gm. daily. On the fourth day she developed haemoglobinuria and was found to be suffering from blackwater. [It is impossible to comment on these cases, but it seems possible that in two of them plasmoquine may have had something to do with the development of methaemoglobinuria]. *W. Y.*

Foy (Henry) & Kondi (Athena). **A Case of Miscarriage following Blackwater Fever.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1941. Jan. 31. Vol. 34. No. 4. pp. 343–346.

Details are given of a case of blackwater fever in a pregnant woman who gave birth to a seven months' child, which died shortly afterwards, thus enabling post mortem examination of the child and the placenta to be made.

The placenta was intact and appeared normal. The blood was withdrawn from it and centrifuged. The serum was reddish-brown and contained haemoglobin and methaemalbumin. The placental blood was loaded with schizonts of *P. falciparum*.

The child had been dead for 5 hours when it was examined. It appeared to be a normal, well formed, seven months' male child. There was no icterus. The serum, which was obtained with difficulty,

was clear, but spectroscopically showed a faint band of haemoglobin in a cell 5 cm. thick; this was, no doubt, traumatic. There was no trace of any methaemalbumin, nor was there any sign of malaria parasites or of pigment in the infant's blood or spleen.

The mother's blood, examined after the birth, contained both haemoglobin and methaemalbumin, and the urine contained haemoglobin and methaemoglobin. From this case it would appear that methaemalbumin does not pass over the placenta to the child.

The authors consider that the absence of any sign of haemolysis in the child may be explained on the hypothesis :—

"(a) That any haemolysins circulating in the mother did not pass through the placenta to the child.

"(b) That any haemolysin present in the mother was only there in sufficient concentration to bring about haemolytic process in the mother, and none was available to produce a haemolytic process in the child.

"(c) Assuming that malaria parasites, or their metabolic products, are necessary for the production of blackwater fever, then the absence of all traces of parasites and malaria pigment from the baby may account for the absence of all signs of haemolysis in the child. Further, sensitization of the mother did not appear to affect the child.

"(d) That the cells of the mother were more liable to haemolysis than those of the child; or had been sensitised by parasites or their metabolic products."

W. Y.

TROPICAL OPHTHALMOLOGY.

A Review of Recent Articles. XXXVII.*

Muco-purulent Conjunctivitis in Ceylon has been described by de Silva.[1] A particularly severe epidemic occurred in Kandy from April to July in 1940, 4,329 patients being treated during that period. The Koch-Weeks bacillus was the micro-organism chiefly responsible for the trouble. In addition to the common necrotic spots of corneal epithelium, corneal ulcers seem to have been met with, and these tended to perforate in debilitated subjects. Painting the lids with 2 per cent. silver nitrate followed by a douche of boracic acid lotion and the instillation of 2 per cent. mercurochrome drops was the routine treatment adopted for the conjunctivitis. (The daily instillation of nitrate of silver drops, 3 grains to the ounce, and the use of a simple eye lotion will usually cure a Koch-Weeks catarrh in five days.)

Trachoma.—Wright[2] has given a further account of his experimental work in connexion with the implantation of filtered and of unfiltered trachoma material on the chorio-allantoic membrane of fowl embryo and on the human conjunctiva. Results as regards the chick membrane were inconclusive. With respect to the human conjunctiva fourteen positive results were obtained in twenty-two individuals inoculated with unfiltered trachoma material. Filtered material was instilled in the normal conjunctival sac of five individuals

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[1] de Silva (K. J. L.). A Study of an Epidemic of Muco-purulent Conjunctivitis at the Eye Institute Civil Hospital, Kandy.—*Jl. Ceylon Branch Brit. Med. Assoc.* 1940. Sept. Vol. 37. No. 3. pp. 159–170. With 1 fig.

[2] Wright (R. E.). Trachoma.—*Brit. Jl. Ophthalm.* 1940. Nov. Vol. 24. No. 11. pp. 547–550.

* For the 36th of this series see Vol. 37, pp. 871–874.

on nine occasions with negative results. One individual, negative on three occasions to filtered material, subsequently proved positive to unfiltered. Though his experiments failed to disclose the nature of the infective agent in trachoma, Wright was able to draw from them some valuable conclusions: (1) Trachoma is not ordinarily a very infectious disease; (2) clinical or experimental observations in connexion with the disease are so liable to fallacious interpretation that they are likely to lead to erroneous conclusions unless very carefully controlled; (3) correct conclusions cannot be drawn from an insufficient number of observations; (4) the nature of trachoma, perhaps more accurately regarded as a congeries of trachomatoid affections of the conjunctiva, still remains obscure. There is a widespread divergence of opinion in the diagnosis, and empirical treatment may often be more dangerous than the condition it attempts to relieve.

The fact that the caruncle and plica semilunaris may often escape treatment in trachoma and may therefore remain a source of irritation after the rest of the conjunctiva is cured has been referred to by OLÁH.[3] He advocates expression of the structures and for this purpose makes an incision in the bulbar conjunctiva, in the neighbourhood of the caruncle, through which he passes one blade of a special expression forceps and is thus able effectively to squeeze the parts.

Cornea.—HAMILTON[4] has reported the occurrence of an epidemic of *superficial punctate keratitis* in Tasmania. Altogether 92 cases were seen. Petechial spots on the skin surface of the lower lid were frequently observed and an actual herpes on the lids was seen in two of the patients. All were completely free from iritis. Painting the conjunctival surface of the lids with 2 per cent. silver nitrate was found to be a most effective treatment.

Iris.—The rôle played by tuberculosis in the aetiology of chronic irido-cyclitis has been discussed by BROOKS, JULER & WILLIAMS[5] The authors investigated forty cases of chronic irido-cyclitis of which most were kept under observation for several years and none for less than six months. Improvement in radiological technique during recent years has rendered the diagnosis and recognition of intrathoracic lesions much easier, and some observers have claimed that many children and nearly all adults possess a focus of infection—usually healed. Clinical and radiological evidence of tuberculosis somewhere in the body was present in twenty-five of the forty patients under review. The authors consider that, while focal sepsis may be a factor in some cases of chronic irido-cyclitis, its importance in the aetiology of the disease has probably been exaggerated. Experience of tuberculin and ultra-violet light in treatment proved on the whole unfavourable. Prolonged rest in bed for a period of at least six weeks was found to be far the most useful therapeutic measure. Local treatment followed the usual lines.

Lens.—The association of certain morbid skin conditions with diseases of the conjunctiva and the cornea (*e.g.*, seborrhoea and acne

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[3] OLÁH (Emil). Encanthis Trachomatosa.—*Arch. Ophthalm.* 1940. Oct. Vol. 24. No. 4. pp. 772–783. With 8 figs.

[4] HAMILTON (J. Bruce). A Survey of Superficial Punctate Keratitis in Tasmania with the Record of a Mild Epidemic.—*Brit. Jl. Ophthalm.* 1941. Jan. Vol. 25. No. 1. pp. 1–17. With 6 graphs & 1 map. [17 refs.]

[5] BROOKS (W. D. Wykeham), JULER (F. A.) & WILLIAMS (E. Rohan). On the Relationship between Chronic Iridocyclitis and Tuberculosis, and the Appropriate Therapy.—*Brit. Jl. Ophthalm.* 1940. July. Vol. 24. No. 7. pp. 317–366. With 22 figs. [44 refs.]

rosacea) is well established ; and it is likely that a systemic disturbance affecting the skin might injuriously affect the lens since both structures have a common origin from the surface ectoderm. MILNER[6] has recorded the development of double *cataract* in a man aged 26 who had been subject to attacks of allergic eczema for many years. A remarkable feature of the case was the exceptionally rapid development of the lenticular opacities in one eye.

The annual Report of the Madras Government Ophthalmic Hospital for the year 1939[7] contains no clinical reports and consists chiefly of tabular statements. The figures it presents are impressive : 38,396 out-patients, 5,572 in-patients, 8,893 operations. Of the operations 2,353 were for senile cataract—112 intracapsular, 2,179 combined capsulotomy, and 62 simple ; 677 lachrymal sacs were excised and 899 operations for the relief of glaucoma were performed. Treatment was given in 240 cases of keratomalacia. Only 116 patients were treated for superficial punctate keratitis during the year. Sun injury to the macula were seen in 54 cases. The cost of the institution amounted to about £10,500. *H. Kirkpatrick.*

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[6] MILNER (J. G.). Allergic Eczema and Cataract.—*Brit. Med. Jl.* 1941. Mar. 8. pp. 356–357.

[7] MADRAS. Annual Report and Statistics of the Government Ophthalmic Hospital Madras, for the Year 1939.—10 pp. 1940. Madras : Govt. Press. [8 annas.]

MISCELLANEOUS.

DIWANY (M.). **Sternal Marrow Puncture in Children.**—*Arch. Dis. in Childhood.* 1940. Sept. Vol. 15. No. 83. pp. 159–170. With 7 figs.

From a study of sterna at different ages it was found that the best site for puncture in children is the centre opposite the second intercostal space. After local anaesthesia a shortened lumbar puncture needle with a movable shield is inserted into the marrow cavity. The shield is fitted at 0·5–0·8 cm. from the point according to age and amount of subcutaneous fat. To obtain sufficient suction a 10 cc. syringe is used to aspirate 0·1–0·2 cc.

The small amount of previous work on normal marrow of children is discussed, and tables are given of the author's results with 5 infants and 10 children. The total nucleated cell count was 75,000–160,000 per cmm. ; myeloid elements predominated ; eosinophil percentage was high (the range was 1·5 to 13) ; lymphocyte percentage was mostly high (12–37·5) ; cells of red series varied between 5 and 18·5 per cent., and were mostly erythroblasts ; myeloblasts were 0·25 to 2 per cent., megakaryocytes were always present. Nine out of ten cases of ankylostomiasis showed marked hyperplasia. Iron therapy after carbon tetrachloride brought the marrow to normal. Ascaris infections produced no characteristic picture. Bilharziasis showed eosinophils between 10 and 15 per cent. in 4 cases and 60 per cent. in one. In two cretins the marrow was hypoplastic, and in one treatment improved the cell picture. *W. P. Kennedy.*

BIERRING (Einar). Haemoglobinometri, Standardisering af Haemometre og Haemoglobinnorm. [**Standardization of Haemometers.**] —*Nordisk Med.* 1940. May 25. Vol. 6. No. 21. pp. 953–958. [78 refs.] English summary.

"Colorimetric determinations of haemoglobin by acid hematin methods (Sahli, Zeiss-Ikon, Newcomer, etc.) are undoubtedly inaccurate for exact scientific work, presumably also for ordinary clinical purposes. The errors involved (partly due to the influence of non-haemoglobin substances in plasma) amount to ± 11% or more. The old carbon monoxide method of HALDANE (or the PALMER modification) still stands in a class above other colorimetric methods. It should be extensively used in laboratories and localities where gas is available. The Danish method (SICCA) based upon colorimetric estimation of reduced haemoglobin may be recommended as a rapid and sufficiently accurate method for the purposes of physicians.

"Standardization of haemometers by reliable gasometric oxygen (or carbon monoxide) capacity methods is still the most accurate procedure at hand. As the ratio Hb colour/Hb gasom. varies individually, a series of different bloods should be standardized by each gasometric standardization. Haemometers should be standardized on 'active haemoglobin'; standardization on 'total haemoglobin' as proposed by AMMUNDSEN seems irrational.

"Calibration of the haemometer scale in vol % O_2 (or g. % Hb.) is logical and simple, but according to our experience physicians are not familiar with these figures. Hence we prefer the Haldane scale, thus expressing our findings in percentage of an arbitrary, but constant figure (18·5), which must not be considered a normal value.

"German haemometers are standardized with a gross systematic error and should be restandardized before use.

"According to international statistics published 1934–1939, the average haemoglobin concentration in men is 113% Hald. (15·6 g.%), in women 99% Hald. (13·6 g.%). The average of Scandinavian investigations 1913–1938 is 110·2% and 97·3% Hald. for men and women respectively. For the sake of simplicity the figures 110% Hald. for men and 100% Hald. for women are proposed as normal values.

"Normal values for children are given based upon the recalculated determinations of WILLIAMSON. The agreement between these figures and actual findings in Scandinavian children is demonstrated. Individual variations of ± 15% are considered normal for children and adults."

NAVARRO (R. J.). **Notes on Blood Platelet Count in Filipinos. (A New Method of counting Platelets in Normal and Abnormal Blood.)**—*Acta Med. Philippina.* 1940. July–Sept. Vol. 2. No. 1. pp. 37–48. [11 refs.]

Many haemorrhagic diseases can be explained as deficiencies of prothrombin or thromboplastin, and there is little evidence that hypocalcaemia is an important factor. No case of hypocalcaemia was found in a study of the blood calcium in Filipinos in health and disease. Accurate diagnosis and treatment of haemorrhagic diseases requires accurate platelet counts; the normal ranges must be known as well as

platelet counts at various stages of the disease. The levels of the platelet count at which haemorrhages are likely to appear or disappear are important. Donors of blood to thrombopenic cases should have their platelets counted to ensure the patient gets full benefit of the transfusion. A few donors were found with low counts though the blood pictures were otherwise normal.

The author withdraws 10 cc. blood using 3–4 drops of 30 per cent. potassium oxalate as an anticoagulant. Exactly 3, 4 or 5 cc. are measured into a calibrated 15 cc. centrifuge tube which is placed upright for 2–4 hours. From midway in the supernatant plasma a white cell pipette is filled to the mark 0·5, then to the mark 11 with saline and is shaken for 3–5 minutes. A counting slide is charged, allowed to stand for 15 minutes and the platelets counted with a dry high power lens in the same manner as red cells. The calculation is modified to suit the dilution, and the platelet number in whole blood found by measuring the cellular pack after centrifuging for an hour and multiplying the count by the plasma volume of 1 cmm. This is permissible as when the platelets are counted they are concentrated in the plasma.

Tables of haemoglobin, red cell, white cell and platelet values are given for 104 healthy males and 34 females. The males averaged 325,000 platelets per cmm. with a range of 204,000–393,000 and the females averaged 338,000 with a range of 180,000–451,000.

W. P. Kennedy.

MacGregor (R. G. Scott), Richards (W.) & Loh (G. L.). **The Differential Leucocyte Count.**—*Jl. Path. & Bact.* 1940. Nov. Vol. 51. No. 3. pp. 337–368. With 10 figs. [29 refs.]

The differential leucocyte count has been used in the assessment of the physiological values of blood in groups of individuals differing in type, or in environment. This experimental and statistical study examines sources of error in the method. Counts on slide films showed variations, particularly in the percentage value of neutrophils and lymphocytes, in different areas of the film. The straight edge, battlement, and cross-section methods of counting on the same film gave variations exceeding 20 per cent. in some cases. Examination of a series of films showed that different cell types differ in distribution, but there is a general relationship between the distribution equation of one type and that of any other type. The relationship varies somewhat for the individual film, but over a series is relatively constant. It was ascertained by counting consecutive segments throughout the films, and then applying Fourier analysis from which graphs were obtained. The graphs correlated the three counting methods with the count made by including all the cells on the film. Thence corrections could be made which rendered the methods comparable. The accuracy of the corrections was tested on a wide series of counts, and the average error was under 3 per cent. When average results obtained from two methods are compared, a correction of as much as 20 per cent. may sometimes result from using this method. The high degree of accuracy would only hold for a series of " standard " films. The battlement edge count, using both edges, approximates most closely to the count of the whole film. Coverslip counts tend to give higher values for neutrophils and lower values for lymphocytes than

the slide film method, and correspond more closely to the straight edge method. [The close statistical argument does not lend itself to a summary which can do the paper justice]. *W. P. Kennedy.*

REYE (Douglas). **A Case of Acute Eosinophilic Leuchaemia.**—*Med. Jl. Australia.* 1940. Aug. 17. 27th Year. Vol. 2. No. 7. pp. 156–157.

An interesting case of eosinophilia with acute symptoms in a boy of 5½ is described. He had been in good health when restlessness, vomiting and abdominal pain occurred. After 8 days he was admitted to hospital; the pain had gone, the liver edge was just palpable, the heart was enlarged, mitral and aortic murmurs were present and there was no oedema. The temperature ranged between 100° and 102°F. and the pulse from 140 to 160 for 3 days; he then became semi-comatose and delirious for 2 days, when he died. The day before death the red cell count was 2·69 millions and the Hb (Sahli) 45 per cent. giving a C.I. of 0·86. The white cell count was 150,000 per cmm. of which 73 per cent. were eosinophils and 14 per cent. neutrophils. The eosinophils were larger than normal with vacuoles and irregular granulation, and appeared as if they were undergoing a severe toxic degeneration. A detailed report of the post mortem findings is given with an able account of the pathological processes concerned. The salient features were that primary bone marrow changes produced an absolute and relative eosinophilia and an excess of neutrophils, at the expense of the red cells. This was followed by subendocardial haemorrhage, clotting in the ventricle with subsequent cardiac and splenic infarcts from fragments of the thrombus. Cardiac damage was followed in turn by pulmonary infarcts, pleural effusion, and congestion in other organs including liver and kidneys. The classification of acute eosinophilic leukaemia was made to align it with the rare syndrome which has been described under that name and which is similar but not identical. *W. P. Kennedy.*

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. 1940. Sept. 28. Vol. 115. No. 13. p. 1121.—**Sensitivity to Liver Preparations.** [Queries and Minor Notes.]

The patient referred to in this note was a woman of 38 years suffering from anaemia. From time to time during the past eight years she has tried to take preparations of liver, parenterally and otherwise, but was unable to continue after 3 or 4 doses owing to the production of allergic symptoms—urticaria, facial flushing and oedema; when given *per os* the liver caused much nausea. Such a condition is, fortunately, rare, but is a serious one in patients suffering from anaemia. The question is what should be done. Desensitization is not likely to be very successful; attempts to control the effect by the use of drugs, ephedrin or barbiturates is not advisable. It may be found that trial of several preparations may result in the discovery of one which is tolerated—a troublesome and perhaps a tedious procedure—failing which there is nothing but to give the liver by mouth and try to overcome the nausea. *H. H. S.*

WIGGLESWORTH (V. B.). **Permeability of Insect Cuticle.** [Correspondence.]—*Nature.* 1941. Jan. 25. Vol. 147. No. 3717. p. 116. [Summary appears also in *Bulletin of Hygiene.*]

Hurst's observation that "apolar substances of low dielectric constant" render the outer lipoid layer of an insect's cuticle more permeable has been confirmed by the author who finds that immersion of the insect in oil—xylol, paraffin, or olive oil, for example—is followed by the appearance of water droplets on the cuticle. "Presumably polar substances of some kind crowd into the oil-water interface as the lipoid layer dissolves, and thus draw out the water droplets." Other mixtures lead to an analogous "effervescence"; Dr. Wigglesworth mentions kerosene and acetone, carbon disulphide and ethyl alcohol, medicinal paraffin and butyl alcohol or pyridine, or the last-named and dodecyl thiocyanate. This observation, and knowledge of the partition coefficient determining the rate at which a substance will enter the tissues of an insect should prove helpful in the selection of insecticides. *H. H. S.*

PEÑA CHAVARRÍA (Antonio) & KUMM (Henry W.). Algunas consideraciones generales sobre la miasis cutanea (tórsalo) en Costa Rica. [**Cutaneous Myiasis (Tórsalo) in Costa Rica.**]—Reprinted from *Rev. Médica.* Costa Rica. 1939. Aug. Vol. 64. pp. 1–7. With 4 figs. [International Health Division of the Rockefeller Foundation. Collected Papers. 1939. Vol. 16. Pt. 2.]

As indicated by the title the remarks on cutaneous myiasis are very general. *Dermatobia cyaniventris,* "ver macaque," is widespread in South America; it is thought that it was first brought in with cattle from Venezuela. The larva attacks cattle, pigs, dogs, monkeys and birds as well as man. The carrier of the eggs is an insect, commonly a mosquito, *Janthinosoma lutzi,* but also *Aëdes angustivittatus* and *Aëd. serratus,* both depicted in this article and carrying the ova, and other mosquitoes, and [though not mentioned in the present paper] *Sarcophaga terminalis, Musca domestica, Stomoxys calcitrans* and the tick *Amblyomma cajennense.* The sites affected in 112 cases seen at the Hospital San Juan de Dios in the decade 1928–37 are given in a table. In nearly half (54) the head and face were attacked, the thigh in 14, the forearm in 8 and the leg in 7. *H. H. S.*

PATIÑO-CAMARGO (Luis). Artropodos hematofagos de la fauna Colombiana. [**Blood-sucking Arthropods in Colombia.**]—Reprinted from *Rev. Facul. de Med.* Bogotá. 1940. July. Vol. 9. No. 1. 38 pp. [25 refs.]

This reprint will be of service to entomologists interested in the geographical distribution of insects. The author has found 24 species [the text states "twenty-two," but 24 are listed and named] belonging to 8 genera of Sabethini, 85 species, ten genera, of Culicini, 21 species of Aëdes, two of which, named *Aëd. quadrivittatus* and *Aëd. pseudodominicii,* are given as new species, 25 species of Anopheles, one of which, *A. squamifemur* is noted as a new species. Among others noted and named are 7 genera of Tabanidae, 21 species, of which 11 were Tabanus, 7 species of Phlebotomus of which two are listed as new

and named *P. osornoi* and *P. colombianus*, and a new variety of *P. monticolus*, named *incarum*; 7 of the family Ixodidae, 4 of them Amblyomma; 4 Argasidae and 2 Reduviidae. *H. H. S.*

BATES (Marston). **Oviposition Experiments with Anopheline Mosquitoes.**—*Amer. Jl. Trop. Med.* 1940. July. Vol. 20. No. 4. pp. 569–583. [13 refs.]

KUMM (Henry W.), KOMP (W. H. W.) & RUIZ (Horacio). **The Mosquitoes of Costa Rica.**—*Amer. Jl. Trop. Med.* 1940. May. Vol. 20. No. 3. pp. 385–422. With 1 graph & 1 map.

HAWKING (Frank). **Sulphanilamide in the Treatment of Climatic Bubo and Similar Conditions.**—*Jl. Trop. Med. & Hyg.* 1940. Dec. 2. Vol. 43. No. 23. p. 271. [Summary appears also in *Bulletin of Hygiene.*]

Sulphanilamide or some member of the sulphonamide group of drugs is now being tried in the treatment of almost any disease and it is only natural that venereal diseases should come within the category, especially since MACCALLUM and FINDLAY found that the mortality was lowered among mice so treated after infection with the virus of L.i.

The author gives brief details of four patients with L.i. The first, after receiving 63 gm. sulphanilamide in 14 days, left hospital with merely slight thickening of the inguinal tissues. Similar results followed in another patient who received 27 gm. in 12 days. A third received 41 gm. in 29 days, and the bubo was incised. The swelling subsided and the patient was discharged. The fourth had two coronal ulcers and climatic buboes, 18 days' history. After 22 days' treatment with sulphone he left hospital, the buboes having subsided. They recrudesced and he returned. In all he received 81 gm. over 7 weeks and still had some residual swelling.

Eleven others had a closely similar history, so that, though some benefit followed, the curative effect cannot be said to have been very remarkable, in fact recovery was, generally speaking, no more rapid than in those who did not receive this form of treatment. With chancroid and granuloma venereum more favourable results were obtained, but the number of venereal cases in which the author has tried the drugs is at present small. *H. H. S.*

CRONKITE (Alfred E.) & LACK (Arthur R.). **Primary Pulmonary Coccidioidomycosis. Experimental Infection with** *Coccidioides immitis.*—*Jl. Experim. Med.* 1940. Aug. 1. Vol. 72. No. 2. pp. 167–174. With 1 text fig. & 4 figs. on 2 plates. [28 refs.]

The authors describe and depict an apparatus by which a guineapig is compelled to inhale an atmosphere laden with dried mycelial spores of *Coccidioides immitis*. Seventy-two animals were exposed for 3–6 minutes, and 23 animals were exposed twice at an interval of a month. Few of the animals, weighed daily for more than 3 months after exposure, showed any loss of weight. Coccidioidin tests were positive in the majority but not in all and the guineapig does not show the high degree of sensitivity that is found in human cases. In man

0·1 cc. of a 1 : 1,000 dilution often gives marked induration and erythema, perhaps vesiculation and a slough, whereas guineapigs usually require 0·1 cc. of full strength coccidioidin.

Early lesions, 8–21 days after inhalation, show as slightly raised, translucent greyish nodules, up to 2 mm. diameter, very like miliary tubercules; microscopically they have the structure of granulomata. The tracheobronchial glands may also show these lesions containing spherules of the fungus. Of 72 animals thus exposed 30 developed primary pulmonary cocidioidomycosis. Photographs show clearly the morbid anatomy and histology of the lesions produced. *H. H. S.*

GUERRA (Pablo). El granuloma a paracoccidioides. Su importancia en patologia pulmonar. [**The Importance of Paracoccidioides Granuloma in Pulmonary Disease.**]—*Rev. de Sanidad y Asist. Social.* Caracas. 1940. Aug. Vol. 5. No. 4. pp. 921–927. With 5 plates. English summary.

This is not a study of pneumoblastomycosis, but a plea for more careful investigation of cases at times regarded as tuberculous. Early diagnosis is essential if treatment is to be successful and some at least of these are looked upon and treated as tuberculous till too late. Four cases are recorded. One was a farmer of 65 years whose illness began a year before he came under observation with small ulcers of the soft palate, troublesome but not painful; a cough and at times spitting of blood. Smears from the buccal lesions revealed Paracoccidioides; *Myco. tuberculosis* was not found. The second was a man of 43 years, who, on account of an ulcer at the base of a tooth, had the latter extracted. The ulcer increased in size and spread along to the mucosa of the upper lip. Troublesome cough continued for years with copious expectoration at times with blood; no T.B. found but paracoccidioides in the sputum and in smears of the buccal mucus. He died two months later and in the lung were nodules and a cavity as large as a hen's egg. The other cases were very similar, local ulcers with expectoration at times blood-stained; absence of tubercle bacillus and presence of Paracoccidioides.

H. H. S.

DE ALMEIDA (Floriano) & ABDALLA (Rosa). Micetomas torácicos. [**Thoracic Mycetomas.**]—*Ann. Facul. de Med. Univ. de S. Paulo.* 1939. Vol. 15. pp. 151–159. With 21 figs. on 13 plates.

In 1936 de Almeida investigated 98 cases of mycetomas according to the site affected and found 68 of the foot, 17 of the leg (including the knee), 6 of head or neck, 4 of the chest, 3 of the abdomen. Since that time he has seen 7 more cases of thoracic mycetoma and brief details are given of each of them. One only need be detailed, as an example. A woman of 30 years was seen in December 1933 and presented numerous but small discrete lesions of the back and right shoulder. By January 1935 these had progressed, but she lived till January 1938 when death occurred with considerable pulmonary involvement.

The authors consider whether the infection starts as a thoracic or a pulmonary lesion, whether it is primarily pulmonary and thence extends through the pleura to the chest wall, or whether the route is the reverse of this, or whether it enters by the alimentary tract (oesophagus) and thence extends to the lungs and chest wall, or finally

whether it is local (*e.g.*, on the foot) and then passes by way of the blood stream to the lungs. The authors conclude that the primary portal of entry is the skin. The article is embellished with some excellent photographs of patients showing this condition and photomicrographs of the histological changes set up. *H. H. S.*

i. WOLF (A.), COWEN (D.) & PAIGE (Beryl H.). **Toxoplasmic Encephalomyelitis. III. A New Case of Granulomatous Encephalomyelitis due to a Protozoon.**—*Amer. Jl. Path.* 1939. Vol. 15. pp. 657–694. With 27 figs. on 6 plates. [Numerous refs.]

ii. ——, —— & ——. **IV. Experimental Transmission of the Infection to Animals from a Human Infant.**—*Jl. Experim. Med.* 1940. Vol. 71. pp. 187–214. With 20 figs. (15 on 5 plates). [13 refs.] [Summaries taken from *Vet. Bull.* 1941. Jan. Vol. 11. No. 1. pp. 21–22. Signed U. F. RICHARDSON.]

i. Four previous cases of protozoan encephalomyelitis have been recorded, and had been provisionally ascribed to *Encephalitozoon* infection, though it was pointed out that they might be due to a toxoplasm, but that this could not be decided until a case became available for experiment. Toxoplasmosis has been recorded in dogs, rabbits, guineapigs, gondis (*Ctenodactylus gondi*), and various other small mammals, reptiles, and birds, and although the organisms have been given different specific names, a number of authors have pointed out that they may represent a single species capable of infecting many hosts. A case is now reported of an infant who became ill when three days old, and developed convulsive seizures, disturbances in respiration and symptoms of involvement of the spinal cord with subarachnoid "block" in the cervical region. The infant died at the age of 31 days. Autopsy revealed a widespread encephalomyelitis characterized by multiple focal areas of inflammation and necrosis, and disseminated miliary granulomas. A protozoan parasite was present, often in great numbers, in the leptomeningeal exudates and in the granulomas and in lesions of the choroid and retina. In comparing the protozoa of this and of one of the previously recorded cases with *Encephalitozoon* infection and toxoplasmosis, it was suggested that morphological differences between *Toxoplasma* and *Encephalitozoon* are insufficient to distinguish between them in sections. Toxoplasms stain easily with all common stains, whilst *Encephalitozoon* only stains well with carbol fuchsin. The lesions of *Encephalitozoon* infection include central necrosis of the granulomas of the central nervous system, whilst this does not occur in toxoplasmosis, or in the recorded human cases. The diffuse inflammatory and necrotic lesions, occurring in these human cases, also occur in toxoplasmic infection of rabbits but not in *Encephalitozoon* infection.

ii. The authors record the infection of rabbits and rats inoculated intracerebrally with material from the brain of the child referred to in i. From the infected rabbits, g.pigs, chickens and monkeys were also infected. The morphology of the organism as seen in experimental animals agreed with the described morphology of a toxoplasm, and the disease produced agreed with the description of experimental toxoplasmosis. Some of the inoculated animals failed to develop severe disease, though in cases in which they were slaughtered infection could be demonstrated. Some of the resistant animals also proved immune to inoculation with strains of animal toxoplasmosis.

This paper gives a very complete account of the morphology of toxoplasms and the lesions of experimental toxoplasmosis, and should be consulted by those interested in the subject.

PINKERTON (Henry) & WEINMAN (David). **Toxoplasma Infection in Man.**—*Arch. Pathology.* 1940. July. Vol. 30. No. 1. pp. 374–392. With 5 figs. [30 refs.]

The blood of a 22-year-old Peruvian at Lima admitted to hospital for fever of one week's duration was found to contain *Bartonella bacilliformis.* Though this infection decreased, the patient died five days after admission. Post mortem examination showed congestion of the organs, focal necrosis and minute nodule formation. In these various lesions in all tissues of the body sections showed numerous organisms which were identified as toxoplasms. The authors point out that this is the first case of toxoplasmosis in an adult, other cases described being in children. The tissues from a case described by HERTIG in 1934 [this *Bulletin*, 1935, Vol. 32, p. 226] as atypical sarcosporidiosis were re-examined. It was found that the organism present was actually a toxoplasm. *C. M. Wenyon.*

MELENEY (Henry E.). **Histoplasmosis (Reticulo-Endothelial Cytomycosis) : a Review. With Mention of Thirteen Unpublished Cases.**—*Amer. Jl. Trop. Med.* 1940. July. Vol. 20. No. 4. pp. 603–616. [37 refs.]

This paper is itself a review of our knowledge of histoplasmosis and the causative organism *Histoplasma capsulatum.* It mentions in all 32 cases but 13 of these are noted for the first time from information given privately to the author. The naturally occurring infection in the dog, as described by DEMONBREUN, and similar infections in other animals are discussed in their relation to the human disease. There is an analysis of the clinical and pathological findings, while the questions of diagnosis, treatment, incidence and method of infection are discussed. It seems clear from the literature that the disease is widespread throughout the world and it is probable that, in the future, cases will be recognized with increasing frequency. *C. M. W.*

CYPRUS. **Nutrition in Cyprus. Activities of the Standing Committee on Nutrition from its appointment to the end of the Year 1938.**—37 pp. 1940. Nicosia : Govt. Printer. [Summary taken from *Nutrition Abstracts & Reviews.* 1941. Jan. Vol. 10. No. 3. pp. 571–572. Signed W. L. SIMPSON.] [Summary appears also in *Bulletin of Hygiene.*]

This is the first contribution towards a comprehensive survey of the nutrition problem in Cyprus. Enquiries were initiated by the Committee to ascertain the actual diet of small wage earners in towns and industrial areas, small farmers, agricultural labourers and schoolchildren, representative sections of the community in 6 districts. Examination of the data showed that the diets of the people were largely deficient in proteins, owing to the non-inclusion of adequate

quantities of milk and meat. It is stated that the Cypriot does not take advantage of the varieties of nourishing foods available at low cost, that the nutritive values of fresh fruit, eggs and other protective foods are not sufficiently appreciated and such items as meat are too expensive to be within reach of the wage-earner. The intake of fat is probably in excess of requirement and, for an island people, the consumption of fish is very low. From enquiries made by schoolmasters, it appeared that the staple diet of school-children consisted of bread, olives, cheese and vegetables daily and a meal of meat and potatoes once or twice a week. Only 30 per cent. of the children drank milk and then only once or twice a week.

Practical measures for the improvement of the nutrition of the people include legislation regulating the quality of the food imported, the establishment of dairies in the chief towns and of soup kitchens in rural districts. Activities of the medical and agricultural departments are also directed towards the improvement of human nutrition. Particular importance is attached to a scheme designed for the encouragement of poultry breeding and the provision of a Home Demonstration Centre in one of the rural areas.

In the 12 appendices are given the chemical composition and nutritive value of Cyprus raisins, wheat and barley, and notes on an uncompleted medical survey made on about 200 children in 4 villages, in two of which the badly nourished children were estimated to be about 45 per cent. of a small number examined. During drought cases of actual starvation have been observed. A complete change in facial expression was seen in those who were given a few days' good food and rest in hospital. The last appendix takes the form of a concise report on the nutrition of workers and of 30 families where the breadwinner was in the employment of the Cyprus Mines Corporation. As a result of these investigations, the Corporation has taken steps towards the construction of bachelor quarters for unmarried labourers, the provision of a large dining room, with kitchen and staff and the supply of nourishing food at low cost to all employees.

In their concluding recommendations the Committee expresses the opinion that the quantitative deficiency of the diet is undoubtedly due to poverty, which only a general improvement in the social and economic conditions, coupled with the development of the industries of the colony, can ameliorate.

BERMUDA. **Report on the State of Nutrition of School Children in Bermuda, 1939.** pp. 12 + appendices. [Summary taken from *Nutrition Abstracts & Reviews.* 1941. Jan. Vol. 10. No. 3. p. 572. Signed W. L. SIMPSON.] [Summary appears also in *Bulletin of Hygiene.*]

The first published report of a committee set up by the Governor in August 1939 to study the state of nutrition among school-children, to ascertain what defects are due to lack of proper food and to suggest remedies, is prefaced by remarks indicating the comparative prosperity of the island during the last 20 years, a position still maintained at the time of the report when a labourer's wage was not less than 10s. a day. Notwithstanding a 50 per cent. increase in population during recent years, the annual number of typhoid cases has been reduced from 37 to nil in 1938 and 1939 and deaths from tuberculosis from 34 to 14 in a year.

During the last 3 years, 3,000 children (white, Portuguese and coloured) in the Central District were medically examined. There were 178 cases of rickets and 1,926 cases of dental caries in this period, the greatest number being in the coloured children.

Defects of vision with chronic conjunctivitis were relatively numerous and are thought to reflect deficiency of vitamin A. In children of every social group infantile rickets had left a permanent mark, which in view of the abundant sunshine, points to absence of some nutritional factors.

A questionnaire survey was made in the homes of 300 school-children covering 1,828 persons or 6 per cent. of the population, including 100 white, 50 Portuguese and 150 coloured families. In the white families, the income per head was 15s. 6d. and the amount available for food was 9s. 6d.; the corresponding figures for the Portuguese families were 23s. 9d. and 16s. 8d., and for the coloured families 12s. 2d. and 7s. 7d.

When a minimum cost diet was calculated, it was shown that 12s. per person per week was the least sum on which an adequate level could be reached. The committee suggests that the sober qualities of the Portuguese go far to explain their superior position. The amounts spent on bread, butter, eggs, fresh fish, fresh meat and fresh vegetables were ascertained and it was found that of the coloured group 21 per cent. spent an adequate amount, 33 per cent. an intermediate amount and 45 per cent. an inadequate amount. In the white families the figures were 31 per cent., 24 per cent. and 45 per cent. and in the Portuguese 32 per cent., 44 per cent. and 24 per cent.

The mineral content of Bermuda vegetables was investigated and an increased production of garden fruit and vegetables is recommended. It is also recommended that the flesh and liver of the shark should be extensively utilised.

Forbes (W. H.), Dill (D. B.) & Hall (F. G.). **The Effect of Climate upon the Volumes of Blood and of Tissue Fluid in Man.**—*Amer. Jl. Physiol.* 1940. Oct. 1. Vol. 130. No. 4. pp. 739–746.

The blood and tissue fluid constitute important links in the chain of mechanisms by which man regulates his body temperature. Earlier workers have noted that changes of climate cause marked variations in the volume of either the blood or tissue fluid and also changes in their composition. In the present paper the authors give the results of 65 determinations of plasma volumes and of "available fluid" in three groups of subjects. The first and main group consisted of ten laboratory workers who were measured both in Boston and Mississippi, the second of white sharecroppers native to Mississippi, and the third of coloured sharecroppers native to Mississippi.

The experimental method was as follows: The subject arrived at the laboratory in the morning fasting and lay down for half an hour. Four cc. of blood were then drawn from the antecubital vein, and 1 gm. of NaSCN dissolved in 20 cc. of water was injected intravenously, followed immediately by 15 mgm. of the dye T1824 dissolved in 10 cc. of water. Four blood samples of 4 cc. each were then drawn at approximately 15-minute intervals, usually from the opposite antecubital vein, followed by two more samples at hourly intervals, the subject remaining resting. The blood was transferred to a haematocrit

tube of 4 cc. capacity containing 1 drop of heparin solution. The samples were centrifuged for an hour, and the concentration of dye in the plasma determined on the Evelyn photo-electric colorimeter. For the determination of the NaSCN, 1 cc. of the plasma was then squirted rapidly from an accurately calibrated syringe into 10 cc. of 10 per cent. trichloroacetic acid and the precipitated proteins were removed by filtering. Eight cc. of the filtrate were added to 3 cc. of 10 per cent. ferric nitrate and the resulting colour read within a minute or two.

The calculations for the plasma volume and the available fluid followed the lines of GREGERSON [*Ibid.*, 1939, Vol. 125, p. 142] and GIBSON [*Jl. Clin. Investigation*, 1938, Vol. 17, p. 153], but the blood volume was calculated from the plasma volume and the haematocrit without making the rather large correction suggested by Gregerson to allow for the greater proportion of plasma in the capillary blood. The " available fluid " was calculated directly from the concentration of NaSCN in the plasma from the last three samples of blood, *i.e.* those taken one, two and three hours after the injection.

From the consistency of the values obtained from different samples in the same experiment and also from repeated determinations on the same individual, the probable error of the method was about 2 per cent. for the plasma volume and between 1·5 and 2 per cent. for the available fluid. In some experiments, however, the plasma, though clear to the eye, gave readings on the colorimeter suggestive of a slight cloudiness, perhaps due to a large meal rich in fat the preceding evening. In these the probable error was 2 to 4 per cent. for the plasma volume, but the available fluid determinations were not affected. Though repeated determinations of available fluid on one subject under the same conditions gave fairly consistent results, there was a disquieting amount of difference between individuals and big changes with changed conditions. It is possible that these variations may be due in part to changes in the permeability of certain cells to NaSCN as well as to changes in the amount of interstitial fluid.

During the period of the observations in the hot and humid " Delta " region of Mississippi, the highest temperature recorded was 101°F. and the lowest 68°F. The mean of the daily high temperatures was 93°F. and of the daily low temperatures, 73°F. These were outdoor temperatures—indoors the fluctuation was undoubtedly less. The mean humidity varied through the day, from 88 per cent. in the early morning to about 60 per cent. at noon and back to 65 per cent. in the evening.

Of the ten white subjects who had determinations made upon them in the north during the winter, nine lost weight, on the average 2 kgm., and one gained 1 kgm. on removing south. In 5 subjects the haematocrit reading increased, in 1 it was unchanged, and in 4 it went down, the average being increased insignificantly. The plasma volume increased in 8 and decreased in 2 subjects, the greatest increase being 420 cc. and the greatest decrease 245 cc. The average went up 4·2 per cent., which is in contrast with other workers' findings of increases up to about 30 per cent. The average plasma volume per kilogram and per square metre of body surface increased a little more (owing to loss of weight), being 6·1 and 4·7 per cent. respectively. As the average haematocrit value was practically unchanged, the percentage change in blood volume was about the same as in plasma volume. In general, those individuals who showed the largest

increases in plasma volume showed decreases in their haematocrit readings, while those whose plasma volume increased but little or decreased in the hot weather showed increases in their haemotocrit readings. There was no consistent change in plasma volume between the first set of determinations made within ten days of arrival in the hotter climate, and the second set made a month later.

The changes in available fluid showed that 7 individuals went down and 3 up, resulting in an average decrease of 1·17 litres, which was 6·9 per cent. below the Boston level of 16·87 litres. The interstitial fluid showed an even greater drop, 1·38 litres, or 12 per cent., from the Boston average of 11·55 litres, but again 8 decreased while 2 increased.

Since the blood volume went up on going to Mississippi and the interstitial fluid went down, it was evident that the greatest change would be found in the ratio of the interstitial fluid to the blood, *i.e.* the ratio of the fluid outside the blood vessels to that inside them. The average decrease in this ratio was nearly 16 per cent.

C. G. Warner.

REVIEWS AND NOTICES.

COVELL (G.) [M.D., D.P.H., I.M.S.]. **Anti-Mosquito Measures with Special Reference to India.** Fifth Edition.—*Health Bull. No. 11. Malaria Bureau No. 3.* pp. ii+58. 1940. Delhi: Manager of Publications. [Annas 8 or 9d.]

In this edition portions of the work have been entirely rewritten and the results of recent work are included. The order has been changed for the better in certain sections and a new Part (IV) on naturalistic control measures has been included; some of the information contained in it was included in other Parts in the previous edition, but new matter on sluicing, intermittent drying and other methods has been introduced. Recent experiences with insecticidal sprays in India are noted. The Bulletin is an improvement on its predecessors, and though intended primarily for use in India, should be in the hands of all those interested in malaria wherever they may be. It is as concise as ever; there are no wasted words. *C. W.*

PURI (I. M.) [M.Sc.(Punjab), Ph.D.(Cantab.), F.R.E.S., etc.]. **Instructions for collecting and forwarding Mosquitoes.** Third Edition.—*Health Bull. No. 13. Malaria Bureau No. 5.* pp. v+57. With 21 figs. on 2 plates. 1940. Delhi: Manager of Publications. [As. 8 or 9d.]

The form and order of the previous edition of this Bulletin are maintained in this third edition, though some of the sections have been rearranged, and the work is brought up to date. Its usefulness is fully maintained. The line illustrations at the end have been re-drawn and improved, but are still not up to the standard which the rest of the Bulletin deserves, though this is a very minor criticism, as the meaning conveyed by the drawings is fairly clear. *C. W.*

CHRISTOPHERS (S. R.) [F.R.S., I.M.S. (ret.)], SINTON (J. A.) [M.D., D.Sc., I.M.S. (ret.)] & COVELL (G.) [M.D., D.P.H., I.M.S.]. **How to do a Malaria Survey.** Fourth Edition. Revised by Lt.-Col. G. COVELL, I.M.S., Director, Malaria Institute of India.—*Health Bull. No. 14. Malaria Bureau No. 6.* pp. vi+208. With 13 plates & 3 figs. 1939. Delhi: Manager of Publications. [Re. 1–12 or 2*s*. 6*d*.]

The fourth edition of this valuable book has been revised by Lieut.-Col. G. Covell and is now issued bound in stiff boards, a useful point in a book which must be constantly used for reference purposes. There has been little change made in the subject matter, but certain information has been brought up to date. *C. W.*

BARRAUD (P. J.) [F.R.E.S., F.Z.S., F.L.S.]. **A Practical Entomological Course for Students of Malariology.** Second Edition. Revised by I. M. PURI, M.Sc. (Punjab), Ph.D. (Cantab.), F.R.E.S., etc.—*Health Bull. No. 18. Malaria Bureau No. 9.* pp. vi+143. With 208 figs. on 18 plates. 1939. Delhi: Manager of Publications. [Rs. 1–12 or 2s. 6d.]

This Bulletin has been revised and the order of the lectures has been slightly rearranged. It remains a full and detailed course of entomology for students of malariology in India, which must be invaluable for students in that country, and in its scope it closely resembles the first edition. The binding might be improved—the book will not lie open, which must be a trial to those who must constantly refer to it in practical work. [See this *Bulletin*, 1935, Vol. 32, p. 303 for a review of the first edition.] *C. W.*

SINTON (J. A.) [M.D., D.Sc., I.M.S.]. **What Malaria costs India.**—*Health Bull. No. 26. Malaria Bureau No. 13.* pp. ii+127. With 1 fig. 1939. Delhi: Manager of Publications. [Annas 14 or 1*s*. 3*d*.]

The subject matter of this Bulletin was originally published in the *Records of the Malaria Survey of India* and reviewed in this *Bulletin*, 1936, Vol. 33, p. 752. The three original papers have now been condensed, largely by omission of matter dealing with conditions outside India, and are published in one volume. The immense importance of the subject to India demands the widest circulation. *C. W.*

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